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ADAPTATION TO PROLONGED BEDREST IN MAN: A COMPENDIUM OF RESEARCH

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16. Abstract

The purpose of this compendium is to gather under one cover the major studies that describe the clinical observations and elucidate the physiological mechanisms of the adaptive process of man undergoing prolonged bed rest. Additional studies are included that provide background information in the form of reviews or summaries of the process. Wherever possible a detailed annotation is provided under the subheadings: (a) purpose, (b) procedure and methods, (c) results, and (d) conclusions. The annotations cover material through December 1973. The annotations are in alphabetical order by first author; author and subject indexes are included. Additional references are provided in the selected bibliography.

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Part of this compendium was written while J. E. Greenleaf was a Polish Academy of Sciences National Academy of Sciences Exchange Postdoctoral Fellow at the Polish Academy of Sciences Laboratory of Applied Physiology, Warsaw, Poland.

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TABLE OF CONTENTS

Page

ADAPTATION TO PROLONGED BEDREST IN MAN: A COMPENDIUM OF RESEARCH

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INTRODUCTION

The purpose of this compendium is to gather under one cover the major studies that describe the clinical observations and elucidate the physiological mechanisms of the adaptive process of man undergoing prolonged bed rest. Additional studies are included that provide background information in the form of reviews or summaries of the process. Wherever possible a detailed annotation is provided under the subheadings: (a) purpose, (b) procedure and methods, (c) results, and (d) conclusions. The annotations cover material through December 1973. The annotations are in alphabetical order by first author; author and subject indexes are included. Additional references are provided in the selected bibliography.

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* Ames Research Associate

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ANNOTATED REFERENCES

1. Ahlinder, S., G. Birke, R. Norberg, L.-O. Plantin, and P. Reizenstein. Metabolism and distribution of IgG in patients confined to prolonged and strict bed-rest. *Acta Medica Scandinavica* 187:267-270, 1970.

Purpose: To investigate the effect of bedrest upon the metabolism and distribution of proteins (IgG).

Procedure and methods: Nine elderly patients, 67 to 88 yr, with cerebral vascular disease (cerebral hemorrhage or thrombosis), who had been confined to bed for long periods, were studied. With one exception, they were virtually unable to move. None had anemia and their hematocrit values varied between 35 and 47 percent. All had normal creatinine values and only slight proteinuria occasionally. Urinary tract infection caused by *E. coli* was present in all cases. The erythrocyte sedimentation rate was slightly to moderately elevated in most cases. Results from these elderly patients were compared with data from normal ambulatory patients.

Results:

Compared with the control cases, in the elderly patients there was a significant decrease in serum total protein, albumin, and plasma volume. IgG concentration was elevated significantly in the elderly patients but the content of IgG was somewhat higher.

The mean catabolic rate of IgG was about twice normal and was significantly elevated from the control patients. The extravascular/intravascular ratio for IgG for the elderly patients was 2.0 to 2.9 compared to 0.9 to 1.5 for the controls.

Conclusions:

The increased catabolism of IgG rendered these patients susceptible to infections.

Plasma volume losses were correlated with body weight losses.

The patient who was able to move and sit out of bed had a nearly normal EV/IV ratio (about 1.2), suggesting the remedial function of upright posture.

It was suggested that the increased extravascular distribution of IgG could have been caused by an impairment of the lymph to retransport proteins due to the reduced muscular function of the inactive patients.

2. Aleksandrov, A. N. and A. K. Kochetov. Effect of 30-day hypokinesia in combination with LBNP training on some indices of the functional state of the cardiovascular system at rest. *Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina* 8:71-72, 1974.

Authors' abstract: The effect of 30-day bedrest and LBNP training on the functional state of the cardiovascular system at rest was studied in two groups of test subjects. A moderate decline in tone and a delay in blood rate flow were noted in the leg vessels (mainly venules). The systolic blood volume decreased. The cardiac output at first decreased and then gradually increased, reaching the initial level by the 30th day, due to an increase in the heart rate. The changes in the EKG T wave suggested metabolic changes in the myocardium. These changes in the EKG were more distinct in test subjects who were daily subjected to LBNP training.

3. Allik, T. A. and L. I. Karpova. Dependence of altitude tolerance of animals on the state of phosphorylation processes. *Kosmicheskaya Biologiya i Meditsina* 1:37-39, 1967.

Authors'abstract: Experiments were carried out on rats to study the effect of hypokinesia on their oxygen consumption at rest, level of amytal-sensitive and amytal-resistant respiration in vivo, activity and altitude tolerance. The effect of a sodium amytal injection on the activity and altitude tolerance was investigated in rats exposed to 6-week hypokinesia and control animals. The exposure decreased oxygen consumption from 159.0 ±6.7 to 94.4 ±23.3 ml per 100 gm of body weight per hour. The part of the amytal-sensitive respiration taken for phosphorylating respiration diminished from 56.8 ±2.16 to 23.7 ±2.0 percent. The activity and altitude tolerance fell in parallel with a decrease of the phosphorylating respiration. An amytal injection made 3-4 days before an exposure to extreme factors (maximum activity and acute hypoxia) elevated both the activity and altitude tolerance. The authors believe that maximum activity and altitude tolerance of an animal organism are in a direct relation to the power of enzymic systems of phosphorylating oxidation.

4. Altman, D. F., S. D. Baker, M. McCally, and T. E. Piemme. Carbohydrate and lipid metabolism in man during prolonged bed rest. *Clinical Research* 17:543, 1969.

Authors' abstract: Bedrest is known to induce an inability of endogenous insulin to lower blood glucose. Hyperinsulinemia results from stimulation by oral glucose, amino acids or tolbutamide. Significant intolerance to glucose may be demonstrated within 2 weeks. An explanation for this is lacking since secretions of growth hormone, cortisol, and catecols are suppressed. In these experiments further characterization of carbohydrate and lipid metabolism was explored.

Observations were made on six male subjects at the conclusion of each of three test periods: a control period of 7 days ad libitum activity, an experimental period of 12 days bedrest, and a 7-day recovery period. Diet was strictly controlled.

A standard insulin tolerance test (0.1 U/g.) resulted in significantly less hypoglycemia ($p < 0.002$) following bedrest. Further, profound hypoglycemic symptoms noted during the control session were not experienced following bedrest. Thus, exogenous as well as endogenous insulin is less effective in lowering blood sugar.

Plasma free fatty acids (FFA) were significantly lower during bedrest and triglycerides significantly higher. This may represent further evidence of norepinephrine depletion as a function of bedrest. The rate of decline of FFA in response to insulin was less marked during bedrest and further demonstrates insulin ineffectiveness.

5. Anashkin, O.D. Effect of hypokinesia, acceleration and reduced nutrition on the state of the blood-coagulation system in man. *Kosmicheskaya Biologiya i Meditsina* 3:89-94, 1969.

Purpose: To investigate the hemostasis system in man during caloric restriction and bedrest.

Procedure and methods:

Experiment 1: Six subjects were ambulatory for 30 days. The first 7 days they consumed 2700 kcal/day. The next 15 days they consumed 1800 kcal/day. The final 7 days they consumed 2700 kcal/day.

Experiment 2: Six subjects were subjected to a 15-day bedrest period (no exercise). They underwent a 7-day control period with 2700 kcal/day, 1800 kcal during bedrest, and the 7-day recovery period at 2700 kcal/day.

Experiment 3: Same as experiment 2 except the subjects were exposed to transverse acceleration ($+G_X$) of 8G for 2 min before and after bedrest.

Antecubital blood was taken in the basal state in the morning.

Results:

Experiment 1: The 15-day dietary restriction period exerted no significant effect on the blood coagulation system.

Experiment 2: Under the combined influence of bedrest and dietary restriction, on day 14 there was (a) a lengthening of thromboplastin time by 18.5 percent, (b) a decrease in activity of the prothrombin complex by 14.5 percent, (c) a decrease in proaccelerin content by 10.2 percent, (d) a lengthening of the thrombin time by 9.3 percent, (e) an increase in blood heparin content by 30.5 percent, (f) an increase in plasma heparin content by 31.8 percent, (g) a tendency to an increase in fibrinolytic activity of the plasma and a decrease in blood tolerance to heparin, and (h) no change in fibrinogen content or the mechanical resistance of thrombocytes.

Experiment 3: Under the combined influence of bedrest, dietary restriction and acceleration on day 14, there was (a) a lengthening of thromboplastin time by 12.5 percent, (b) a decrease in activity of the prothrombin complex by 11.5 percent, (c) a decrease in proaccelerin content by 10.5 percent, (d) an increase in plasma coagulation time by 42.1 percent, (e) an increase in blood heparin content by 34.4 percent, (f) an increase in plasma heparin content by 43.8 percent, (g) a reduction in blood tolerance to heparin by 17.9 percent, and (h) an increase in antithrombin activity 13.8 percent. On the eighth recovery day, plasma coagulation time remained elevated but pro-accelerin content and the activity of the prothrombin complex remained at their decreased levels.

Conclusions: The decrease in the coagulating capacity of the blood after 14 days bedrest with caloric restriction was due primarily to an increase of blood heparin. The addition of acceleration to bedrest and caloric restriction results in a longer recovery time for plasma coagulation time than with bedrest and caloric restriction alone. The decrease in the coagulating capacity of blood in man during bedrest is apparently associated with a decrease in the synthesis of procoagulants by the liver due to a general decrease in the metabolic processes and to an increase in the blood heparin content.

6. Asher, R. A. J. The dangers of going to bed. *British Medical Journal* 4:967-968, 1947.

Author's comments:

It is always assumed that the first thing in any illness is to put the patient to bed. Hospital accommodation is always numbered in beds. Illness is measured by the length of time in bed. Doctors are assessed by their bedside manner. Bed is not ordered like a pill or a purge, but is assumed as the basis of all treatment. Yet we should think twice before ordering our patients to bed and realize that beneath the comfort of the blanket there lurks a host of formidable dangers. . . . . There is hardly any part of the body which is immune from its dangers.

The maintenance of one position allows the collection of bronchial secretions which encourage the development of hypostatic pneumonia. Further, the absence of exercise and the diminished respiratory excursion prevent the re-expansion of collapsed or diseased lung.

Thrombosis and thrombo-embolism are some of the most disabling and lethal catastrophes that bedrest can bring to a patient. One theory of phlebothrombosis is that it starts with endothelial damage caused by the weight of the leg on the bed compressing emptied calf veins. It is significant that Hunter, Sneedon, and others, performing post-mortem examinations of the veins of the calf in middle-aged and elderly people who had been in bed a considerable time, found thrombosis of the calf veins in 53 percent of the cases.

The frequency and dangers of bedsores are too well known to need much comment. The pressure points on the heels are often a source of great pain and misery to the pateint even if the skin is still unbroken.

The contraction of some muscles and the stretching of others are complications which may cause considerable crippling. Foot-drop is the commonest and stiffness and flexion of the knee joints probably the next. The weakness and wasting of the general skeletal musculature and the restriction of the excursion of the joints are often manifest in the hobbling, painful gait of the convalescent patient.

When bones are not used, the calcium drains from them, and this disuse osteoporosis can be a serious matter, especially in the elderly.

The drain of calcium from the bones causes an increased liability to urinary calculi, and both kidney and bladder stones are sometimes in part due to bedrest. A patient, particularly male, with a perfectly normal urinary tract can find difficulty in using a bottle because of the horizontal position of the body coupled with the nervousness and embarrassment felt on attempting an unnatural, uncomfortable, and unfamiliar method of micturition. Getting a patient out of bed may turn him from an incontinent person to a clean one.

After a few days in bed, minor dyspepsias and heartburn may be noticed and the appetite is often lost. Constipation usually occurs. Its causes are the absence of muscular movement, the change of environment, and the difficulties of evacuating the bowel in a hospital bedpan. On a bedpan, the patient is unable to use his abdominal muscles and his nearness to fellow patients discomforts him. Precariously engaged in balancing himself, he sits there, poised unhappily above his own excrement in great dissatisfaction and distress. Quite often complete intestinal obstruction can develop from retained feces, and when enemata fail to shift the scybala, digital removal has to be practiced—a procedure as unpleasant for the evacuator as for the evacuee.

In the ataxic diseases, such as disseminated sclerosis or tabes dorsalis, even a short spell in bed may produce a deterioration of mobility which takes weeks to overcome, and any length of time in bed may leave a patient bedridden many years before the natural course of the disease would have made him so.

Lastly, consider the mental changes, the demoralizing effects of staying in bed. At the start it may produce fussiness, pettiness, and irritability. At a later stage, a dismal lethargy overcomes the victim. He loses the desire to get up and even resents any efforts to extract him from his supine stupor. The end result can be a comatose, vegetable existence in which, like a useless but carefully tended plant, the patient lies permanently in tranquil torpidity. Many hours of half-sleeping and dozing are less beneficial than a few hours of deep sleep, and they encourage a certain confusion of mind.

Bedrest is anatomically and physiologically unsound: "Look at a patient lying long in bed. What a pathetic picture he makes! The blood clotting in his veins, the lime draining from his bones, the scybala stacking up in his colon, the flesh rotting from his seat, the urine leaking from his distended bladder, and the spirit evaporating from his soul!"

"Teach us to live that we may dread unnecessary time in bed. Get people up and we may save our patients from an early grave."

7. Balakhovskiy, I. S., V. T. Bakhteyeva, R. V. Beleda, Ye. I. Biryukov, L. A. Vinogradova, A. I Grigor'yev, S. I. Zakharova, I. G. Dlusskaya, R. K. Kiselev, T. A. Kislovskaya, G. I. Kozyrevskaya, V. B. Noskov, T. A. Orlova, and M. M. Sokolova. Effect of physical training and electric stimulation on metabolism. *Kosmicheskaya Biologiya i Meditsina* 6:68-72, 1971.

Purpose: To investigate the effect of isometric exercise, induced by electrical stimulation, and isotonic exercise on various metabolic processes during 30 days bedrest.

Procedure and methods: Fifteen healthy men were divided into five groups of three men each: series A—group 1; series A—group 2; series B—group 1 (isotonic exercise (500 kcal/day) for 24 days, then lower body negative pressure on days 25 through 30. The exercise was accomplished by walking on a treadmill with the body suspended in the horizontal position); (see Stepantsov *et al.,* 1972). series B–group 2 (no exercise control); and series B–group 3 (isometric exercise by electrical stimulation of the muscles).

Analyses were made of serum glucose, cholesterol, phospholipids, nonesterified fatty acids, hydrocortisone, body hemoglobin, urea bilirulim, creatinine, protein fractions, and urinary adrenaline/noradrenaline, dopamide, 17-hydroxycorticosteroids, sodium, potassium, calcium, total nitrogen, and aldosterone.

Results: In series A, in the subjects of both groups there was a slight decrease in the urinary concentrations of adrenaline, noradrenaline, and dopamine by the end of bedrest. Group 1 exhibited a decrease in the blood content of erythrocytes, hemaglobin, and hematocrit. Group 2 did not show the changes exhibited by group 1 but during the period of LBNP they did show a decrease in RBC count, a loss of leukocytes, hemoglobin, and hematocrit.

In series B, during bedrest the control group exhibited an increase in blood cholesterol that was somewhat less elevated with isometric exercise and reduced below control levels by isotonic exercise. Blood glucose decreased in all three groups. By the 16th day of recovery, only cholesterol remained elevated in the isotonic and no exercise groups; the isometric group had greatly reduced cholesterol levels. Total hemoglobin content was reduced in the no exercise and isometric groups but did not change with isotonic exercise. Aldosterone excretion was high in the isotonic group and unchanged in the no exercise group and not measured in the isometric group. 17-Hydroxycorticosteroid excretion in the urine was increased about equally in all three groups.

Tests with a water load made on the second day of recovery revealed essentially the same response in all series B groups: there was an increased elimination of water and sodium compared to presumably pre-bedrest data.

Conclusions: Both isometric and isotonic exercise training during bedrest are capable of at least partially modifying the negative effects. Their use prevented an increase in the content of nonesterified fatty acids and cholesterol and reduced the increase in blood glucose during recovery. Training with LBNP appeared to have no appreciable effect on the metabolic variables measured in this study.

8. Bassy, E. J., T. Bennett, A. T. Birmingham, P. H. Fentem, D. Fitton, and R. Goldsmith. Changes in the cardiorespiratory response to exercise following bed-rest in hospital patients. *Journal of Physiology (London)* 221:79P-81P, 1971.

Purpose: To determine whether unselected subjects, exposed to a surgical operation, underwent similar, adverse cardiovascular response to exercise as selected, healthy subjects.

Procedure and methods: Twenty male subjects, 18 to 58 yr, were admitted to an orthopedic hospital for removal of a cartilage from one knee. They comprised two groups: (a) those kept in bed for 14 days after surgery and (b) those kept in bed for 4 days after surgery and then went home for 10 days with a plaster cast on the operated leg (at home, these subjects were not confined to bed). Both groups returned to the hospital after 2 weeks and performed daily exercise.

Heart rate at a standard oxygen uptake of 1.1 liter/min on a bicycle ergometer was taken as the index of cardiovascular response to exercise.

Results: Two weeks after the operation, group (a) showed a consistent (8 of 9 subjects) increase in heart rate (from 110 to 123 beats/min), and in group (b) six subjects showed an increase, 5 subjects a decrease and one subject no change (the group mean increased from 111 to 114 beats/min).

Conclusions: Early ambulation promotes cardiovascular fitness. Measurable, but reversible impairment occurs in the cardiorespiratory response to exercise when hospital patients are confined to bed.

9. van Beaumont, W., J. E. Greenleaf, and J. Davis. Erythrocyte volume with $+G_Z$ centrifugation in women after 15-days' bed rest. Aerospace Medical Association Preprints, 1974, p. 61.

Purpose: To reevaluate conflicting results on the effect of acceleration on the mean corpuscular volume (MCV).

Procedure and methods: Eight female subjects (22-34 yr) were exposed to $+G_Z$ centrifugation after a 13-day control period (C), after 15 days of bedrest (BR), and after 3 days of ambulatory recovery (R). The average centrifugation time with a maximal acceleration of +3.0G was 1164 sec (C), 594 sec (BR), and 1041 sec (R). Antecubital venous blood samples were obtained without stasis just before and directly after each centrifugation test, which consisted of three consecutive runs with 5-min rest periods between runs. Microhematocrit determinations were made by centrifugation for 10 min at 11,000 rpm. Analyses for hemoglobin (Hb) and red blood cell count (RBC) were performed and the MCV was calculated from the ratio Hct/RBC, while the MCHC was derived from Hb/Hct.

Results: The percent changes in RBC, Hb, and hematocrit (Hct) and the actual pre- and postcentrifugation measurements of MCV and MCHC are as follows:

Variable	Control		Bedrest		Recovery	
RBC	+6.8		+2.4		+ 9.0	
Hb	+6.9		+ .8		+10.0	
Hct	+7.0		+2.4		+10.1	
	Pre-	Post-	Pre-	Post-	Pre-	Post-
MCV (μ^3)	93.1	94.2	92.1	92.8	92.1	92.7
MCHC (percent)	33.3	33.3	33.6	33.0	33.2	33.0

Conclusions: These results from 24 centrifugation tests do not support the earlier findings that there is a decrease in the MCHC and that the erythrocyte volume changes significantly with centrifugation, but are in agreement with recent observations that *in vivo* the red cell volume in healthy individuals remains constant during intense physical stress. Neither centrifugation of moderate intensity, 15-day bedrest, or short intensive exercise changes the volume of the human red cell. The change in plasma volume during centrifugation can be accurately calculated by the use of this equation:

$$\text{Percent } \Delta\text{PV} = \frac{100}{100 - \text{Hct}_{\text{pre}}} \times \frac{100(\text{Hct}_{\text{pre}} - \text{Hct}_{\text{post}})}{\text{Hct}_{\text{post}}}$$

10. van Beaumont, W., J. E. Greenleaf, and L. Juhos. Disproportional changes in hematocrit, plasma volume, and proteins during exercise and bedrest. *Journal of Applied Physiology* 33:55-61, 1972.

Authors' abstract: The interrelationships between the changes in plasma volume, hematocrit, and plasma proteins during muscular exercise and bedrest were investigated. Proportionally, the changes in hematocrit are always smaller than the changes in plasma volume. For this reason, changes in the concentration of blood constituents can only be quantitated on the basis of plasma volume changes. Percent changes in plasma volume can be calculated from hematocrit readings by application of the proportionality factor 100/(100-Hct). During short periods of intensive exercise, there was a small loss of plasma proteins. With prolonged submaximal exercise, there was a net gain in plasma protein which contributes to stabilization of the vascular volume. Prolonged bedrest induced hypoproteinemia; this loss of plasma protein probably plays an important role in recumbency hypovolemia.

11. van Beaumont, W., J. E. Greenleaf, H. L. Young, and L. Juhos. Plasma volume and blood constituent shifts during $+G_Z$ acceleration after bedrest with exercise conditioning. *Aerospace Medicine* 45:425-430, 1974.

Authors' abstract: The purpose of the present study was to investigate the influence of isometric and isotonic exercise during bedrest on plasma volume (PV) and blood constituents during $+G_Z$ acceleration in seven young men. During bedrest, PV decreased between 8.0 and 11.5 percent. During centrifugation before bedrest, the average decrease in PV was between 10.7 and 13.2 percent, with concomitant plasma protein losses of 2.6 to 3.7 percent, and albumin losses of 1.2 to 4.6 percent; after bedrest, the corresponding changes with centrifugation were between −6.3 to −7.1 percent, −1.1 to −2.0 percent, and +2.4 to −3.1 percent, respectively. The average acceleration tolerance during the prebedrest control runs was 1,129 ± S.E. 27s, while after bedrest, the mean tolerance was 817 ±S.E. 31s ($p < 0.05$). For comparative purposes, additional hematological changes with centrifugation were evaluated from nine different hypovolemic, ambulatory subjects. During $+G_Z$ acceleration there was an isotonic loss of plasma fluid (8.6 to 11.2 percent) with respect to serum sodium, potassium, chloride, creatinine, and osmolarity; however, serum glucose concentration increased between 6.3 and 19.3 percent. It is concluded that during acceleration (a) the mean reduction in PV and protein contents after bedrest is about half as great as during the control runs before bedrest; (b) isometric and isotonic exercise during bedrest have no effect on the decrease in PV and protein contents during centrifugation; (c) during $+G_Z$ acceleration, in hypohydrated ambulatory subjects, there is an isotonic loss of plasma fluid; (d) centrifugation tolerance was significantly reduced following bedrest; and (e) the two exercise regimens had no statistically significant effect upon postbedrest centrifugation tolerance; however, both isometric and isotonic exercise reduced the average $+G_Z$ tolerance decrement by 85 - 100s.

12. Beregovkin, A. V., P. V. Buyanov, A. V. Galkin, N. V. Pisarenko, and Ye. Ye. Sheludyakov. Results of investigations of the cardiovascular system during the aftereffect of 70-day hypodynamia. *Problemy Kosmicheskoy Biologii* 13:221-227, 1969.

Authors' abstract: This article sets forth data on the aftereffect of prolonged hypokinesia and evaluates the effectiveness of the preventive measures taken against its unfavorable effects on the basis of the stability and degree of the changes in the circulatory system. During 1-3 days before the start of the experiment and in the afterperiod until the changes noted had vanished, the subjects were examined by a therapist who used generally accepted clinical methods; electrocardiograms were recorded, hemodynamics was studied by N. N. Savitskiy's method at rest, after measured physical exertion, and during the passive orthostatic test. The results of five series of experiments in which 15 subjects participated were studied. Electrocardiographic examination during the afterperiod showed a change in the bioelectrical activity of the heart and disturbance of metabolic processes in the myocardium. The hemodynamic changes indicated disturbance of cardiovascular regulation and poor adaptation of the system to physical exertion and orthostatic disturbances. These shifts were most distinct and protracted in the series I subjects ("pure hypokinesia"). The smallest changes were found in the individuals of series III, where hypokinesia was combined with physical exercises on a treadmill.

13. Beregovkin, A. V. and V. V. Kalinichenko. Reactions of the cardiovascular system during 30-day simulation of weightlessness by means of antiorthostatic hypokinesia. *Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina* 8:72-77, 1974.

Purpose: To investigate the reactions of the cardiovascular system during simulated weightlessness by means of antiorthostatic hypokinesia where the subjects head is lowered 4° relative to the horizontal.

Procedure and methods:

Group	Subject	Age (yr)	Principal experimental conditions
1st	Sh-s	21	Hypodynamia in an antiorthostatic position (angle of inclination 4°) for 30 days. Daily performance of groups of physical exercises in special trainer with vertical "treadmill" twice a day for 1 hr from the 1st through the 24th day, daily work with trainer for 1 hr and exposure to LBNP with peak values 36-44 mm Hg for 2.5 hr from 26th through 30th days.
	Ni-v	19	
	B-v	19	
2nd	S-v	29	
	K-n	26	
	Ne-v	24	Control group
3rd	O	25	Daily electric stimulation of muscles of lower leg, hip, abdomen, and back (V. Yu. Davidenko) for 30 min twice a day.
	Mv	32	
	D	33	

A rigorous hypodynamia regime was adhered to. Body rotation relative to the longitudinal axis and restricted movements of the arms necessary for waiting on oneself. The subjects received preserved foods from a special diet (about 3200 cal). Water consumption was not restricted. The angle of inclination of the functional bed was selected in such a way to ensure a well-expressed blood distribution effect without thereby creating inconveniences associated with involuntary body movement along an inclined plane. Four times during the course of hypodynamia, functional tests were performed with the creation of LBNP of 35 and 45 mm Hg for 10 min at each pressure level.

The investigations were made in the mornings immediately after the subjects awoke, except for the first day of antiorthostatic hypokinesia when they were carried out 3 and 6 hr after onset of the experiment. During the background period, there were two investigations during the first three days of the experimental period–daily, at subsequent times not less than once in 4 days, and in the recovery period–1, 2, 3, 4, and 6 days after a changeover to a free regime. In the background and recovery periods records in a lying position served as a point of departure in carrying out an active orthostatic test and were made each minute with shifting of the subject into a standing position for a period of 5 min. Polycardiograms (PCG) and mechanocardiograms (MCG) were recorded on a polygraph consisting of the N. N. Savitskiy mechanocardiograph, operating in unison with a phonocardiograph.

Results: During the background period, the studied hemodynamic indices were within the limits of the physiological norm. By the end of the first day in the first-group subjects, there was a clearly expressed hyperemia of the skin on the face, neck, and ears, but at the same time this was not observed in the other subjects. After 5 to 7 days, there was adaptation of the circulatory system to an unusual position without a significant difference in the groups. With the onset of training by exposure to LBNP, respiratory arrhythmia became the same as during the background period. The expulsion period corresponded to the proper levels for a particular pulse rate with a single peculiarity: in the first group subjects on the days of training with LBNP, the expulsion period did not decrease in accordance with the increase in pulse rate, but increased. The arterial pressure parameters varied within the narrow limits of physiological normalcy with individual considerable deviations in first and second group subjects. The tone of the main vessels increased insignificantly. The systolic and minute volumes changed insignificantly. Restoration of hemodynamics with transition to a free regime in groups carrying out prophylactic measures occurred on the average in 2 days, whereas in the control group the frequency of cardiac contractions and the systolic volume were not restored during the 9 days of observation. The reaction to an orthostatic load in the subjects were more clearly expressed in the recovery period (19-22 hr after transition) than during the background period. In subjects in the experimental groups (first and third), the reaction to an orthostatic load was restored approximately twice as rapidly as in the control group. In the overall evaluation of the reaction to the orthostatic test using the indices of general hemo- and cardiodynamics a restoration was noted on the average in the first group after 4 and 7 days, in the second group after 7 and 3 days, and in the third group after 3 days.

Conclusion: By means of antiorthostatic hypokinesia, it was possible to reproduce some weightlessness effects with an adequate approximation. It can be considered established that the physical training, LBNP, and electric stimulation of the muscles used in the experiment exerted a positive influence on the state of the cardiovascular system of the subjects during the hypokinesia period. This influence was clearly manifested with transition to a free regime in a more rapid restoration of the functional state of the cardiovascular system.

14. Bird, A. D. The effect of surgery, injury, and prolonged bed rest on calf blood flow. *The Australian and New Zealand Journal of Surgery* 41:374-379, 1972.

Author's abstract: Using strain-gauge plethysmography, the resting calf blood flow, mainly a measure of muscle blood flow, has been estimated in control subjects, in patients during and after surgical procedures, and in patients during prolonged bedrest following surgery or operation. During general surgical procedures, the calf blood was reduced by 38 percent of the preoperative values. After operation, there was a progressive fall in calf blood flow, the lowest values showing a reduction averaging 58 percent of the preoperative flow. The reductions in blood flow were associated with an increase in peripheral resistance, indicating that local vasoconstriction was the cause of the reduced flow. Low calf blood flow was also shown to occur in patients who were confined to bed for long periods after injury or operation. It is suggested that by reducing venous return, the decreased calf blood flow during and after surgery, and during prolonged bedrest may be a factor in the development of deep vein thrombosis in surgical patients.

15. Birkhead, N. C., J. J. Blizzard, J. W. Daly, G. J. Haupt, B. Issekutz, Jr., R. N. Myers, and K. Rodahl. Cardiodynamic and metabolic effects of prolonged bed rest AMRL-TDR-63-37, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, May 1963.

Authors' abstract: To evaluate the circulatory and metabolic effects of prolonged inactivity, urinary nitrogen, calcium, and phosphorus excretion were measured in four healthy trained men on a constant diet (2500 cal. 77 gm protein, 74 gm fat, 385 gm CHO, 1724 mg calcium) during 42 days of continuous supine bedrest. Maximum oxygen uptake and hemodynamic response to 70° head-up tilt and supine bicycle exercise at three and six times resting O_2 uptake levels were determined pre- and post-bedrest. Urinary excretion of calcium and phosphorus increased within the first 6 days. Calcium excretion reached a peak approximately twice control values after 24 days. No significant change occurred in urinary nitrogen. Tolerance to 70° head-up tilt and physical work capacity decreased following bedrest, but a satisfactory cardiodynamic response to supine exercise was maintained. Physical work capacity returned to near pre-bedrest values after 18 days of retraining.

16. Birkhead, N. C., J. J. Blizzard, J. W. Daly, G. J. Haupt, B. Issekutz, Jr., R. N. Myers, and K. Rodahl. Cardiodynamic and metabolic effects of prolonged bed rest with daily recumbent or sitting exercise and with sitting inactivity. AMRL-TDR-64-61, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, Aug. 1964.

Authors' abstract: Eight healthy men were studied to evaluate the modifying effects of supine or sitting exercise or quiet sitting on the circulatory and metabolic consequences of prolonged bedrest. They were fed a weighed formula-type diet of 2500 cal (78 gm protein, 71 gm fat, 390 gm carbohydrate, and 1.630 gm calcium) throughout the study. Urinary nitrogen, calcium, and phosphorus excretions were determined from 6-day pooled samples. Four subjects remained at recumbent bedrest for 24 days except for 1-hr daily lying (two subjects) or sitting (two subjects) bicycle ergometer exercise, and four subjects remained at recumbent bedrest for 16 hr and sat quietly in a chair for 8 hr daily for 30 days. All subjects underwent physical training for 18 days before and after these periods of inactivity. Just before and after the period of inactivity, the response to 70° head-up body tilt and maximal O_2 uptake were determined. One hour daily of lying or sitting exercise prevented the deterioration of physical work capacity previously found during 6 weeks of bedrest alone. Supine exercise did not prevent the development of tilt intolerance but sitting exercise was effective in one of two subjects. Eight hours daily of quiet sitting added to bedrest resulted in only minor decreases in physical work capacity and maintained tilt tolerance in three of four subjects. Supine or sitting exercise or quiet sitting did not prevent the increased urinary calcium excretion. There was no consistent change in nitrogen balance.

17. Birkhead, N. C., J. J. Blizzard, B. Issekutz, Jr., and K. Rodahl. Effect of exercise, standing, negative trunk and positive skeletal pressure on bed rest-induced orthostasis and hypercalciuria. AMRL-TR-66-6, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, Jan. 1966.

Authors' abstract: Tilt intolerance and hypercalciuria were induced in healthy subjects (fed weighed diets) by 18-32 days continuous bedrest in a Metabolic Ward. The effect of supplementing bedrest with daily supine bicycle exercise (2 or 4 hr), quiet standing (3 hr), or longitudinal supine skeletal pressure on orthostasis and urinary calcium was determined. Tilt tolerance was evaluated by blood pressure and heart rate response to 10 min of 70° head-up tilt and urinary calcium excretion by analysis of 3- or 6-day urine collections. Supine bicycle exercise was ineffective in significantly reducing tilt intolerance or hypercalciuria. Standing decreased orthostasis in three of five subjects and decreased urinary calcium in four of five subjects. Longitudinal skeletal pressure decreased hypercalciuria in one of two subjects, but did not improve tilt tolerance. Intermittent lower body negative pressure during bedrest in one subject impeded development of orthostasis but increased urine calcium. Three hours daily standing is the minimum effective duration for reversing bedrest-induced tilt intolerance and hypercalciuria while supine bicycle exercise is not a practical method for obtaining similar effects.

18. Birkhead, N. C., G. J. Haupt, J. J. Blizzard, P. A. Lachance, and K. Rodahl. Effects of supine and sitting exercise on circulatory and metabolic alterations in prolonged bed rest. *Physiologist* 6: 140, 1963.

Authors' abstract Prolonged bedrest (6 weeks) resulted in increased urinary excretion of calcium (Ca) but not nitrogen (N), orthostatic intolerance and decreased maximal 0_2 uptake. To further study these effects, similar metabolic and hemodynamic measurements were made in four healthy trained men before, during, and following 24-day continuous bedrest, except for 1 hr daily of bicycle exercise in supine (two subjects) or sitting (two subjects) position. Urinary Ca increased by the second week and reached levels twice control values. Decreased tolerance to 70° head-up body tilt also developed, but maximal 0_2 uptake and pulse response to exercise were unaltered. One hour of daily supine or sitting exercise was sufficient to maintain physical work capacity but did not prevent orthostatic intolerance or increased urinary Ca loss resulting from bedrest.

19. Birkhead, N. C., G. J. Haupt, B. Issekutz, Jr., and K. Rodahl. Circulatory and metabolic effects of different types of prolonged inactivity. *American Journal of the Medical Sciences* 247:243, 1964.

Authors' abstract: Previous studies in this laboratory have shown that continuous supine bedrest for 42 days in healthy subjects resulted in (1) marked impairment in the ability to tolerate headup body tilt despite the presence of demonstrable arteriolar vasomotor activity and an adequate cardiodynamic response to supine exercise, (2) decreased physical work capacity as measured by maximal oxygen uptake and heart rate response to submaximal work, and (3) an approximate twofold increase in urinary excretion of calcium but no change in nitrogen balance.

The present study was undertaken to determine the effects of (1) daily lying or sitting exercise for 1 hr at 600 kpm/min during 24 days bedrest and (2) a 16-hr lying, 8-hr sitting schedule for 30 days on these basic effects of bedrest. Four healthy male subjects were studied on each regimen. All were hospitalized in a metabolic ward and fed a weighed formula-type diet (2500 cal, 77 gm protein, 74 gm fat, 385 gm carbohydrate, and 1700 mg calcium). Twenty-hour urine collections were pooled into 6-day samples and analyzed for nitrogen, creatinine, calcium, and phosphorus. For 18 days before and after inactivity, all subjects trained on the bicycle ergometer for 1 hr daily at 600 kpm/min. Immediately before and after inactivity, maximal oxygen uptake was determined and response to 70° headup tilt measured by direct recording of intra-arterial and central venous pressures. All subjects remained in nitrogen equilibrium. Daily lying or sitting exercise maintained physical work capacity but not tilt tolerance. Quiet sitting for 8 hr daily maintained tilt tolerance but physical work capacity decreased slightly. Neither regimen prevented increased urinary calcium excretion during inactivity. These results indicate that the three effects (tilt intolerance, deconditioning, and hypercalciuria) are separable and not all attributable to inactivity per se.

20. Birkhead, N. C., G. J. Haupt, and R. N. Myers. Effect of prolonged bedrest on cardiodynamics. *The American Journal of the Medical Sciences* 245:118-119, 1963.

Authors' summary: Hypodynamic states such as prolonged bedrest have profound effects on the circulatory system which result in transient orthostatic intolerance and decreased exercise capacity. These effects are attributed to decreased sympathetic activity on the arterial and venous components of the circulation. Hemodynamic data supporting this hypothesis are scarce. To study this problem further, observations were made in four healthy young men before and after 6 weeks of complete continous supine bedrest. The subjects were hospitalized in a metabolic ward on a constant measured diet (daily intake 2500 cal, 78 gm protein, 71 gm fat, and 388 gm carbohydrate) throughout the study. After an 18-day conditioning period before and after the 6-week bedrest, maximum aerobic work capacity and exercise pulse response was determined. Immediately before and after bedrest, cardiac catheterization was performed. The circulatory response to 70° head-up body tilt and supine exercise at oxygen consumptions of 3 to 4 and 5 to 6 times resting values were determined. Central venous and peripheral arterial pressures were recorded by strain-gage manometers connected to indwelling catheters and cardiac output was measured by the indicator dilution technique. During the post-bedrest study, one subject developed nodal tachycardia which precluded continuing the catheterization. In the other three subjects, tolerance to 70° head-up tilt was markedly reduced after bedrest to 3-1/4, 1-1/2, and 3/4 min. Although there was interindividual variation, average increases in cardiac output after 3 min of the two levels of supine exercise were 116 and 208 percent before and 107 and 148 percent of resting values after bedrest. Heart rate and systolic and diastolic pressures at rest and during exercise were higher in every instance during the post-bedrest study. In spite of this, calculated vascular resistances were not systematically altered by bedrest. Maximum aerobic work capacity and heart rate response to exercise returned to near pre-bedrest values when measured after 18 days of reconditioning. These data indicate that despite prolonged bed-rest which resulted in orthostatic intolerance, a satisfactory cardiodynamic response to supine exercise occurred and arterial vasomoter function could be demonstrated. This study provides further evidence implicating decreased venomotor tone as a predominant factor in the circulatory alterations produced by bedrest.

21. Biryukov, Ye. N., L. I. Kakurin, G. I. Kozyrevskaya, Yu. S. Koloskova, Z. P. Payek, and S. V. Chizhov. Change in water-salt metabolism during 62-day hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 1:37-39, 1967.

Purpose: To study the dynamics of water and mineral metabolism in healthy men during bedrest with and without physical exercise.

Procedure and methods:

Six healthy men (22 to 36 yr) were used as subjects and most had engaged in sports. They remained in bed for 62 days and three men were non-exercise controls.

The exercise group performed 15-30 min of work in the morning and 1 to 2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased.

The training was performed utilizing springs and large rubber bands. Bands with resistances of 7.5 to 15 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercise. The average energy cost of the exercises was about 7.3 kcal/min, (500 to 1000 kcal/day) with a total working time of 75 to 150 min/day.

Calorie intake was 3000 to 3500 kcal/day.

Results:

Water consumption during bedrest fell from 36 to 22-24 ml/kg. Exercise had no effect on water consumption.

There was a marked rise in electrolyte concentration during the first 4 weeks and by the end of the 8th week of bedrest had returned to their initial levels. Exercise had no effect on electrolyte excretion.

Serum sodium rose progressively and reached its highest concentration on the 40th day of bedrest; exercise had no effect.

In the exercise group, serum calcium did not change over bedrest, but in the non-exercise group, calcium rose and reached its peak values by the 25th day.

X-ray densitometry showed the greatest loss of bone density in the non-exercise group.

The exercise group lost the most body weight.

Conclusions The water-electrolyte losses during bedrest are due to the shift to the hydrostatic position and are not due to reduction in physical exercise. Calcium loss can be retarded by physical exercise.

22. Blotner, H. Effect of prolonged physical inactivity on tolerance of sugar. *Archives of Internal Medicine* 75:39-44, 1945.

Purpose: To investigate whether the carbohydrate metabolism was disturbed in a group of nondiabetic patients who had been confined to bed for relatively long periods of time.

Procedure and methods:

The subjects were 86 nondiabetic persons, 70 adults and 16 children. Dextrose tolerances, measured on patients who had been in bed in a hospital from 4 weeks to 13 yr, were compared with tolerances made on 10 normally active adults and on 11 active children.

A standard dose of 100 gm of dextrose was used for the adults and a dose of 50 gm for the children who weighed less than 34 kg and 75 gm for those over 34 kg. Sugar concentration in blood and urine was measured during fasting and at intervals of 30 min, 1, 2, and 3 hr after ingestion. In 10 cases, sugar tolerance was measured after the formerly bedridden patient had been ambulatory for 2 to 6 months.

The patients received the routine house diet, which consisted of approximately 250 gm carbohydrate, 70 gm protein, and 75 gm of fat. The daily calorie intake was about 2000 kcal.

A family history of diabetes was obtained for only two adult patients and none of the children had a history of diabetes in the family.

Results:

In general, there was a diminished sugar tolerance in the patients who had been confined to bed. Of the 70 adults, 63 had definitely diminished sugar tolerance curves. In all these cases there was no sugar in the fasting urine samples. After sugar ingestion, there often was high levels of sugar in the urine, but frequently the urine was free of sugar when blood levels were 200 to 250 mg.

Often the patients who were in bed the longest had the highest blood sugar curves. Some of the patients who were more active in bed or in chairs did not have as greatly elevated blood sugar curves as those whose activity was more restricted. One arthritic patient, age 67, who had been in bed for 7 yr, had a normal sugar tolerance.

Of the 10 long-term bedridden patients, after 2 to 6 months of recovery, six had normal values, two were marginal, and two were unchanged.

In the bedridden children, all showed diminished sugar tolerance, but their blood sugar levels did not rise as high as the adults.

The concentration of sugar in the blood obtained from capillary puncture of the finger was practically identical with the concentration of sugar obtained from radial arterial blood.

In many of the patients, the arteriovenous differences in sugar concentration were greater than normal. This suggests that even though patients are physically inactive, their muscles utilize sugar normally.

Conclusion: It is suggested that during prolonged physical inactivity the pancreas is at rest because in this state there is not the demand for rapid storage and utilization of sugar that there is in active persons. Consequently, there may ensue diabetic-like reactions to dextrose tolerance tests even with normal fasting levels of blood sugar.

23. Bogachenko, V. P. State of psychic activity in subjects during prolonged confinement to bed. *Problemy Kosmicheskoy Biologii* 13:171-174, 1969.

Author's abstract: Distinct changes in psychic state took place in subjects who were strictly confined to bed and did not perform physical exercises or receive medication during this confinement. These changes were less distinct in the group of individuals who performed especially designed physical exercises. In the two series of experiments in which a composite set of prophylactic measures was applied, practically no changes in the psychic sphere were detected. The decisive factor in the development of the neuropsychic disturbances was the forced immobility.

24. Bohnn, B. J., K. H. Hyatt, L. G. Kamenetsky, B. E. Calder, and W. M. Smith. Prevention of bedrest-induced orthostatism by 9-alpha-fluorohydrocortisone. *Aerospace Medicine* 41:495-499, 1970.

Purpose: To evaluate the effect of 9-alpha flurohydrocortisone on plasma volume during bedrest.

Authors' abstract: Eight healthy volunteers were evaluated during two 10-day bedrest periods and two 10-day ambulant periods. Studies were metabolically controlled. Subjects received 0.4 mg of 9-alpha-fluorohydrocortisone daily during one bedrest period and an identical placebo during the other. At the end of drug bedrest, mean plasma volume was 348 ml greater than at the end of placebo bedrest. This greater plasma volume resulted in heart rate responses to tilt and exercise and heart rate recoveries from exercise which were similar to pre-recumbency responses. These results suggest that there is a relationship between plasma volume decrease during bedrest and the alterations in cardiovascular response to gravitational stimuli and exercise seen following bedrest.

25. Brannon, E. W., C. A. Rockwood, Jr., and P. Potts. The influence of specific exercises in the prevention of debilitating musculoskeletal disorders; implication in physiological conditioning for prolonged weightlessness. *Aerospace Medicine* 34:900-906, 1963.

Purpose: To determine the type, frequency, and duration of exercise required to maintain the healthy state of the musculoskeletal system during 60 days of bedrest.

Procedure and methods: Thirty healthy men (18 to 22 yr) in good physical condition were subjected to 60 days of bedrest during which time they were divided into five groups of six subjects, with the following exercise routines performed daily: group 1 – normal, ambulatory activity and performed the 5 BX exercise routines twice daily for 11 min each; group 2 – bedrest with isotonic exercise with 10 lb of resistance with 10 repetitions; group 3 – bedrest and isotonic exercise with no resistance and 10 repetitions; group 4 – bedrest and isometric exercise with dynamic tension for 6 sec and 10 repetitions; and group 5 – bedrest and no exercise. Movement limited to turning, sitting, eating, washing, handwork, and bedpan.

Other measurements taken were routine blood counts, hemoglobin, hematocrit, prothrombin time, sedimentaion rate, blood calcium, phosphorus, alkaline phosphatase, potassium, sodium, creatine, creatinine, chloride, cholesterol, urea nitrogen, glucose, total protein, albumin, albumin/globulin ratio, body weight, basal metabolism, vital capacity, EKG, visual acuity, reaction time, muscular strength, and extremity girth measurements.

Results: There were no significant changes in any of the blood chemistry values. The daily urinary outputs for each subject did not fluctuate appreciably for the 60-day bedrest period. Changes in body weight were: group 1, +1.4 kg; group 2, −2.0 kg; group 3, −4.2 kg; group 4, −3.0 kg; and group 5, −2.7 kg. There were no significant alterations in pulse rate, blood pressure, BMR, vital capacity, EKG, visual acuity, or reaction time.

The loss in muscle mass and strength became apparent after the second week of bedrest. In group 5 (bedrest, no exercise), there was no loss of handgrip strength, but forearm atrophy averaged 0.7 cm. Groups 3 and 4 sustained slight losses in strength and thigh girth with substantial losses in both in group 5 (thigh lost 2.5 cm). All subjects showed a decrease in the girth and strength of the calf muscles; group 3 lost 2.5 cm and group 5 lost 2.7 cm. The average loss of thigh and calf girth was less in groups 3 and 4 when the prescribed exercises were done four to six times daily compared to those subjects who performed them only twice daily.

Group 5 subjects continued to have some pain and instability even 40 days after the completion of bedrest.

Conclusions: The isometric exercises appeared to maintain muscular integrity about as well as the isotonic exercises with applied resistance and better than the isotonic exercises without weights.

26. Briggs, M. H., P. Garcia-Webb, and T. Cheung. Androgens and exercise. *British Medical Journal* 3:49-50, 1973.

Abstract: Previous studies have shown that serum androgen concentrations increase significantly in response to maximal exercise in athletes and normal male students. Serum androgen determinations in immobilized patients seem to illustrate the converse effect. The mean serum androgen concentration (ng/ml) in 4 healthy men was 4.4 (range 3.6–5.0 ng/ml); in 4 ambulatory male patients was 5.5 (range 2.8–9.4 ng/ml), and in 15 immobilized male patients was 0.6 (range 0.2–1.5 ng/ml). Thus, serum androgen levels in the normal men and in the ambulatory male patients were all within the previously reported normal range, but were markedly depressed in the immobilized, severely ill male patients. These findings are opposed to those of serum corticosteroids in immobilized patients, which are raised significantly. The decreased androgen levels may be the result of a reduced testicular response to gonadotrophins or decreased hypothalamic-pituitary gland activity. It would seem that both extremes of physical activity have significant effects on serum androgens in man.

27. Browse, N. L. Effect of bedrest on resting calf blood flow of healthy adult males. *British Medical Journal* 1:1721-1723, 1962.

Authors' summary: The resting calf blood flow has been measured daily, for varying periods, in 29 healthy male patients. Twelve were living the normal ward life, the rest were confined to bed. The resting calf blood flow, principally a measurement of the calf muscle blood flow, was remarkably constant. There was no day-to-day variation in the 12 active patients nor did the rate of flow change when another 12 patients were confined to bed for 12 hr and a further 5 for periods of 2 to 5 days. The calf blood flow reaches its resting level before an hour of rest has elapsed, and this explains why early ambulation after surgery has no effect on the incidence of postoperative, deep-vein thrombosis.

28. Buhr, P.A. On the influence of prolonged bodily inactivity on the blood sugar curves after oral glucose loading. *Helvedica Medica Acta* 30:156-175, 1963.

Author's summary: Oral double blood sugar loading tests with twice 20 to 30 gm of glucose were performed on 22 patients who, on account of various ailments, had been bedridden for 7 weeks to 5 yr. Unexpectedly, two cases of true diabetes mellitus and one person with probable oxyhyperglycemia were discovered. One subject with probable hepatic disease refused further investigation. The remaining nondiabetic patients showed that the longer the period of inactivity the more frequent were abnormal forms of glucose tolerance curves, but one only fulfilled all our criteria for diabetes mellitus, while several others were interpreted as diabetes suspects. After a duration of 3 months, bedrest alone has a retarding effect on the assimilation of glucose. Recuperated activity improves glucose tolerance curves. Also, the oral blood sugar loading tests with small doses of glucose are unreliable on patients with prolonged and *complete* physical inactivity. Diabetic or almost diabetic curves appear under these circumstances in nondiabetic subjects. However, in patients who are able to perform daily some little exercise while staying in bed, even 20 weeks of *incomplete* inactivity changes our blood sugar tolerance curves so little that there is no risk of diagnostic mistake.

29. Burkhart, J. M. and J. Jowsey. Parathyroid and thyroid hormones in development of immobilization osteoporosis. *Endocrinology* 81:1053-1062, 1967.

Authors' abstract: The experiment was designed to determine whether the osteoporosis observed with immobilization is the result of local factors or develops in response to circulating hormones, which are more effective in the immobilized part. The hormones considered were those from the thyroid and parathyroid glands. Thirty adult dogs were divided into four groups; intact, parathyroidectomized, thyroidectomized, and thyroparathyroidectomized. The right hind limbs were immobilized in a single hip spica cast, which was replaced at weekly intervals. After 3 to 12 weeks, the tibia and one metatarsal were removed from the immobilzed and nonimmobilized limbs of each animal, and quantitative microradiographic studies were carried out; the degree of porosity, bone formation, and bone resorption were measured in the midshaft of these two bones. The pCO_2 and pO_2 and pH of arterial and venous tibial blood were measured in selected animals. The results showed that after 3 weeks there were both roentgenologic evidence and microradiographic evidence of osteoporosis in the immobilized limb of intact animals; the increase in bone resorption continued for 8 weeks, at which time bone formation rose and showed further increase at 12 weeks. Osteoporosis developed only in the intact animals; this indicated that the osteoporosis of immobilization depends on the presence of parathyroid and thyroid glands. The results further indicated that bone resorption or increased bone turnover produces a change [illegible] blood metabolites as evidenced by increase pCO_2 and decreased pH of bone blood in the immobilized limbs of the intact animals. No such changes appeared in the control limbs or in the immobilized limbs of the animals lacking parathyroids or thyroids or both. There appears to be a local factor produced by disuse which may act by increasing the sensitivity of the bone to normal circulating levels of thyroid and parathyroid hormones; alternatively, a local change in the disused area may increase the effectiveness of the hormones in their action on normal bone. Further experiments are being carried out in an attempt to discover which of these alternatives is more likely.

30. [illegible]anov, P. V. [illegible] N. V. Pisarenko. Prevention of the adverse effect of hypokinesia on the [illegible] 8-82, 1967.

Purpose: To evaluate the effect of intermittent cuff inflation and various physical exercises as preventive measures for bedrest deconditioning.

Procedure and methods: Thirteen healthy men (22 to 26 yr) underwent 10 to 12 days of bedrest. Three series of investigations were performed: series A; control without preventive measures; series B: compression of the lower limbs at 2-hr intervals at a pressure of 60-75 mm Hg for 10-15 min with an antigravity suit; and series C: a complex of physical exercises were used before, during, and after bedrest.

Conclusions: Intermittent limb compression and physical exercise are effective in preventing the unfavorable effects of bedrest on the cardiovascular system. Better results were obtained by the physical training. The favorable effects of physical exercise may be related to the physiological hypoxemia.

31. Buznik, I. M. and S. A. Kamforina. Elimination of creatinine in the urine during prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 7:60-64, 1973.

Authors' abstract: Elimination of creatinine in the urine was examined in six test subjects exposed to a 94-day bedrest experiment. Three of them performed physical exercises with energy expenditures of 250 cal/day. Beginning with the second week of hypokinesia, the elimination of creatinine with the urine increased. Beginning with the 50th day of the experiment, the test subjects who had performed no exercise exhibited a greater increase in elimination. These changes were traced using the CN index (urine creatinine nitrogen:total urine nitrogen X 100). This index is more precise than the creatinine coefficient and the absolute values reflect changes in creatinine metabolism and can be recommended for their evaluation. An increase in the CN index gives evidence that catabolic processes predominate in the muscle tissue. Physical exercises do not eliminate but alleviate these changes, exerting a normalizing effect on the metabolism. There is a distinct correlation between creatinine excretion, total urine nitrogen, and diuresis.

32. Campbell, J. A. and T. A. Webster. Day and night urine during complete rest, laboratory routine, light muscular work and oxygen administration. *Biochemistry Journal* 15:660-664, 1921.

Purpose: To determine the effect of day and night cycles on nitrogen metabolism.

Procedure and methods: One male subject, 28 yr, was subjected to three 5-day periods of (a) complete bedrest, (b) 6-1/2 hr of ordinary laboratory routine, and (c) 1-1/2 hr ordinary laboratory routine plus 5 hr of work (13,500 kg-m/hr on a bicycle ergometer).

Authors' summary:

Total nitrogen was decreased at night under all routines specified. Ammonia was increased at night. Creatinine, urea, uric acid, and amino acids were excreted in greater amounts during the day than during the night.

Acidity of the urine was distinctly higher during the night under all routines. Activity out-of-bed hastened the excretion of acid.

The phosphate tide at night is considered to be due to the increased acidity of the urine. It did not appear to be connected with muscle or nerve metabolism in particular.

The sulphur was evenly distributed between day and night.

The increase of acidity at night is considered to be due to delayed excretion of certain fixed acids formed in the cells during the day.

Administration of 35-40 percent of oxygen did not affect the composition of the urine.

33. Cardus, D. Effects of 10 days recumbency on the response to the bicycle ergometer test. *Aerospace Medicine* 37:993-999, 1966 (see Cardus, D., W. C. Beasley, and F. B. Vogt. A study of the possible preventive effects of muscular exercises and intermittent venous occlusion on the cardiovascular deconditioning observed after 10 days bed recumbency. NASA CR-692, 1967).

Author's abstract: Eleven healthy men were submitted to three periods of 10-day bed recumbency with intervening 3-week periods of normal activities. In one of the bed recumbency periods, the subjects were submitted to bedrest alone. In another period, half of the subjects followed a program of intermittent venous occlusion in the lower extremities. In the third bed recumbency period, the treatments were switched. Bicycle ergometer tests were conducted before and after bed recumbency periods. Heart rate, pulmonary ventilation, and metabolic gas exchange measurements were done at different workload levels. After bed recumbency, the heart rate at rest and during exercise was higher than before bed recumbency. The oxygen intake at the heart rate of 160 was diminished after bed recumbency. No changes were observed in pulmonary ventilation, frequency of breathing, and mechanical efficiency. The effect of muscular exercises and intermittent venous occlusion as preventive treatments for the altered heart rate response observed after bed recumbency seemed to be different for the two groups of subjects. Possible interpretations of this observation are discussed.

34. Cardus, D. O_2 alveolar-arterial tension difference after 10 days recumbency in man. *Journal of Applied Physiology* 23:934-937, 1967.

Authors' abstract: This study was conducted on seven healthy men whose ages varied from 21 to 25 yr. Measurements of the O_2 alveolar-arterial tension difference ($(A\text{-}a)DO_2$) were made in the supine position before and after 10-day bed recumbency. The O_2 and CO_2 partial pressures were determined with the Clark and Severinghaus electrodes, respectively. The alveolar O_2 partial pressure was calculated from the alveolar equation. The $(A\text{-}a)DO_2$ increased in all the cases. The average $(A\text{-}a)DO_2$ before recumbency was 9 mm Hg. The average $(A\text{-}a)DO_2$ after recumbency was 19 mm Hg. This increase in the $(A\text{-}a)DO_2$ was due to a change in the Pa_{O_2} which varied from 103 mm Hg before recumbency to 94 mm Hg after recumbency. The mechanism by which the $(A\text{-}a)DO_2$ increases with prolonged bed recumbency is discussed with regard to information obtained by other investigators from experiments conducted in animals or human subjects during anesthesia.

35. Cardus, D., C. Vallbona, F. B. Vogt, W. A. Spencer, H. S. Lipscomb, and K. B. Eik-Nes. Influence of bedrest on plasma levels of 17-hydroxycorticosteroids. *Aerospace Medicine* 36:524-528, 1965.

Authors' abstract: Plasma levels of 16-hydroxycorticosteroids at 0800, 1200, 1600, 2000, and 2400 hr were determined on six healthy subjects who were submitted to two 3-day periods of bedrest. During the first period, the subjects were in bedrest only. During the second, a program of isometric exercises was added to bedrest. The determinations of 17-hydroxycorticosteroids in plasma were made with a modification of the Peterson method and the Porter-Silber technique. During bedrest the peak level at 0800 seemed a little lower than the peak values observed while the subjects were ambulatory, but the difference was not statistically significant. Bedrest did not modify the circadian rhythm of 17-hydroxycorticosteroids in plasma. During the period that isometric exercises were added to bedrest, the rhythm and the levels of 17-hydroxycorticosteroids were normal. One to two days bedrest has no effect on the circadian rhythm of 17-hydroxycorticosteroids.

36. Chan, S. S. Excretion of creatine and creatinine in adult male subjects during immobilization and ambulation. Master of Science Thesis, Texas Woman's University, Denton, Texas; May 1965.

Author's summary: From the review of literature, it became apparent that only limited research work has been done on creatinine metabolism and almost none on creatine metabolism during bedrest immobilization.

According to *table VII*, the subjects of this study show no statistically significant changes on urinary creatinine excretion during ambulation, bedrest, or recovery periods. The creatinine excretion values for subject L were slightly higher during the period of bedrest, but it is questionable that this had any statistical significance. It was also noted that this man had the greatest loss of total urinary nitrogen excretion during the period of bedrest, which could be the reason for the slight increase in urinary creatinine excretion during the period of bedrest.

There was a statistically significant rise in the excretion of creatine in three out of the five subjects during the bedrest period. The average urinary creatine excretion for most of the subjects during ambulation ranged from 0 to 0.015 gm/day. It also was apparent that, during the recovery period, the excretion of urinary creatine went back to the normal excretion values of 0 to 0.028 gm. This agrees with the general concept that creatine is not excreted in significant amounts in the urine of normal adult males.

37. Chase, G. A., C. Grave, and L. B. Rowell. Independence of changes in functional and performance capacities attending prolonged bedrest. *Aerospace Medicine* 37:1232-1238, 1966.

Purpose: To determine if the increment in submaximal pulse rate following bedrest is necessarily accompanied by a decrement in work capacity and objectively determine maximal oxygen uptake and how these changes are interrelated. Does oxygen uptake at a self-determined endpoint of exhaustion on the bicycle ergometer equal maximal oxygen uptake as objectively determined on a treadmill? Does the application of in-bed isotonic exercise have any effect on submaximal pulse ratio work capacity, and maximal oxygen uptake following the stress of prolonged bedrest? To determine whether two types of isotonic leg exercise during bedrest would prevent orthostatic intolerance.

Authors' summary: Eighteen young men were studied before and after 15- and 30-day bedrest to examine the effects of absolute bedrest and recumbent exercise during bedrest on the pulse rate response to submaximal work, cardiovascular functional capacity (max $\dot{V}_{O_2}$), physical work capacity, and orthostatic tolerance. Changes in the submaximal pulse rate as a result of the conditions of this study did not predict the trend in either work capacity of max $\dot{V}_{O_2}$ whereas changes in work capacity occurred independently of changes in max $\dot{V}_{O_2}$ and vice versa. The highest $\dot{V}_{O_2}$ attainable during exercise to exhaustion on a bicycle ergometer underestimated max $\dot{V}_{O_2}$ 4 to 23 percent. When recumbent exercise was carried out during bedrest, the difference in the highest $\dot{V}_{O_2}$ attainable on a bicycle ergometer and the max $\dot{V}_{O_2}$ was decreased after bedrest by an increment in $\dot{V}_{O_2}$ during the bicycle test. Unless max $\dot{V}_{O_2}$ was increased during bedrest, subjects had decreased adaptability to posture afterward.

38. Chazov, Ye. I. and V. G. Ananchenko. The status of anticoagulating mechanisms under conditions of prolonged hypokineses. *Aviation and Space Medicine,* Akademija Meditsinskikh Nauk, SSSR, Moscow, 1963, pp. 414-415.

Purpose: To investigate the anticoagulating mechanisms during bedrest.

Procedure and methods: Twelve male volunteers (19 to 20 yr) were studied during (a) 3 days of bedrest (4 subjects), (b) 20 days of bedrest (4 subjects), and (c) 4 subjects remained at prolonged (?) bedrest but underwent a number of systematic physical exercises. Measurements made were free heparin in the blood, blood fibrinolytic activity, plasma heparin tolerance, and thromboelastography.

Results:

After 3 days of bedrest, the blood heparin level fluctuated between 5-6 units/ml, plasma heparin tolerance was 15-17 min, blood fibrinogen was 250-300 mg/100 ml, and fibrinolytic activity (25-30 percent) was normal.

After 20 days of bedrest, there was a definite increase in the anticoagulating and lytic properties of the blood, which leads to lessening the possiblities for thrombus formation. Fibrinolytic activity increased to between 50 and 100 percent and blood heparin in three subjects rose 2 units/ml. In three subjects, plasma heparin tolerance rose from 15-17 to 22-26 min, but heparin tolerance declined in the fourth subject from 17 to 12 min. In all four subjects, blood fibrinogen dropped to 100 to 250 mg/100 ml.

During prolonged bedrest with physical exercise, there was no increase in the blood fibrinolytic activity or its content of free heparin.

Conclusions: The observed increases in the anticoagulating and lytic properties of the blood during bedrest may be the defensive reactions to conditions that increase thrombus formation or they may be the reaction to the "stress" of prolonged bedrest. Physical exercise during bedrest can be a factor that prevents the rise in the anticoagulating and lytic properties of the blood.

39. Cherepakhin, M. A. Normalization of physiological functions during bedrest by means of physical exercises. *Kosmicheskaya Biologiya i Meditsina* 2:37-42, 1968.

Purpose: To determine the influence of isometric and isotonic exercise for the prevention of the after effects of 62 days of bedrest.

Procedure and methods:

Six healthy men (22 to 36 yr) were used as subjects and most had engaged in sports. They remained in bed for 62 days and 3 men were non-exercise controls.

The exercise group performed 15-30 min of work in the morning and 1 to 2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased.

The training was performed utilizing springs and large rubber bands. Bands with resistances of 7.5 to 15 kg were used to exercise the shoulder muscles and bands between 15 and 50 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercise. The average energy cost of the exercises was about 7.3 kcal/min (500 to 1000 kcal/day), with a total working time of 75 to 150 min/day.

The caloric intake was 3000 to 3500 kcal/day.

Results:

At the end of the bedrest period, the non-exercise control subjects decreased strength of 14 to 24 percent, isotonic endurance reduced by 26 to 55 percent, and isometric endurance reduced by 24 percent. They exhibited tachycardia, paleness, and shortness of breath. Orthostatic tolerance was reduced.

At the end of the bedrest period, the subjects who exercised exhibited an increase in strength by 19 to 21 percent, isotonic endurance increased 25 to 27 percent, and isometric endurance increased by 20 to 30 percent. Orthostatic tolerance was higher (no data given).

Conclusions:

Due to the physical training, which was performed for 2-1/2 hr/day, the test subjects retained the strength of their shoulder and leg muscles, their resistance to static and dynamic stresses, and their tolerance for overloads.

The positive influence of physical exercise on the tolerance to orthostatic actions, mineral saturation of the bones, and the immunobiological defense of the organism was demonstrated.

In making up a program of physical exercises for conditions including long hypokinesia, particular attention must be given to exercises that increase endurance. The non-exercising control subjects lost their endurance first.

To retain tolerance for overloads, it is important to utilize isometric exercises. The method of performing these exercises requires further investigation.

40. Cherepakhin, M. A. Effect of prolonged bedrest on muscle tone and proprioceptive reflexes in man. *Kosmicheskaya Biologiya i Meditsina* 2:43-47, 1968.

Purpose: To investigate the effect of 62 days bedrest and physical training during bedrest on muscle tone and on the proprioceptive reflexes in man.

Procedure and methods:

Six healthy men (22 to 36 yr) were used as subjects and most had engaged in sports. They remained in bed for 62 days and three men were non-exercise controls.

The exercise group performed 15-30 min of work in the morning and 1 to 2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased.

The training was performed utilizing springs and large rubber bands. Bands with resistances of 7.5 to 15 kg were used to exercise the shoulder muscles and bands between 15 and 50 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercise. The average energy cost of the exercises was about 7.3 kcal/min (500 to 1000 kcal/day), with a total working time of 75 to 150 min/day.

The caloric intake was 3000 to 3500 kcal/day.

Muscle tone was measured with a "Sirmai" myotonometer in the middle third of the shin, along the axis of symmetry of the tibialis anterior muscle, in the middle third of the quadriceps femoris and biceps brachii muscles. Muscular tone was measured during a maximal contraction of that particular group of muscles. Circumferential measurements were made of the shoulder, shin, and hip.

Proprioceptive reflexes were induced by a dynamotensometric hammer. The following reflexes were investigated: mandibular, bicipital, and tricipital muscles of the shoulder, the knee, and Achilles tendon.

Results:

Muscle tone gradually decreased during bedrest in both groups of subjects, but more so in the non-exercising men.

By the end of bedrest the circumferences of the lower legs had decreased more (up to 1 cm more) in the no exercise subjects. The changes in circumference of the hips and arms were not different from the control subjects.

All subjects lost weight during the bedrest period, but the exercisers lost more (−1.1 kg) than the control subjects (−0.2 kg).

During bedrest the strength of the exercisers increased by 20 percent whereas the strength of the control subjects decreased by 24 percent. No relationship could be detected between muscle tone and proprioceptive reflexes. The latent periods of the reflexes were exceptionally stable during all experiments. Their duration was dependent upon the length of the reflex path.

Conclusions: The authors believe that the reasons for the decrease in muscle tone, the decrease in the circumferences of the distal parts of the extremities, and the tendency to a decrease in body weight were the same, that is, a redistribution of the water-salt equilibrium within the body, particularly to tissue fluid loss.

41. Cherepakhin, M. A. Effect of a reduced diet and hypokinesia on human tolerance to static loads. *Kosmicheskaya Biologiya i Meditsina* 4:67-72, 1970.

Author's abstract: Three series of experiments, each 15 days in duration, were run; there were 18 subjects in the age group 24-37 yr. In all the experiments the subjects were fed a ration of 1800 cal/day consisting of lyophilized foods. In the first series the motor activity regime was unrestricted. In the second series the subjects adhered to a rigorous bed confinement. In the third series the conditions differed from those in the second in that before and after the experiments the test subjects were exposed to accelerations in a chest-to-back direction (8 g) for a period of 120 sec. A diet of lyophilized foods (15 days, 1800 cal) with a normal motor activity regime exerts no effect on man's tolerance to static loads. Hypokinesia in the form of bedrest confinement for 15 days with a diet of lyophilized foods in a quantity of 1800 cal/day exerts a negative effect on man's tolerance to stress. A static functional test consisting of isometric exercise can be recommended for predicting man's tolerance to accelerations. This test can be made in small-volume chambers, in bed, in a fixed position, or in a spacesuit. It is concluded that the dietary restriction was of less importance for maintaining performance than the proposed optimum motor activity regime.

42. Chukhlovin, B. A. and S. A. Burov. Resistance to infection under conditions of hypodynamia. *Problemy Kosmicheskoy Biologii* 13:116-122, 1969.

Purpose: To investigate the nonspecific resistance to infection of the body during bedrest.

Procedure and methods:

Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest.

Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of air cuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt-table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

The study was divided into two parts: (a) an investigation of indices of the organism's nonspecific resistance (phagocytic activity of leucocytes, bactericidal properties and titer of complement and titer of serum properdin, lysozyme activity of saliva, bacteriostatic property of skin, etc. and (b) an investigation of indices of specific immunity to infection and the degree to which the organism is inseminated with pathogenic and saprophytic microflora.

The material for investigation (blood, saliva, smears, and smear impressions from the skin and mucous membranes) was taken 2 or 3 times at intervals of 7-10 days before the start of bedrest, thereafter every 10-20 days during bedrest, and 2-3 times after its termination.

Results:

The most significant changes during bedrest were observed in leucocyte phagocytic function. (a) There was a distinctly weaker ability of the blood cells to capture microorganisms during the first 2-3 weeks of bedrest, with a subsequent rise in this function to nearly initial levels and then another decline by the end of 60 days of bedrest and lasting through the termination of bedrest. (b) There was a decrease in the absorption function of the blood neutrophils during the first month of bedrest with a gradual rise to the initial level by the end of bedrest. (c) The third type of disturbance to neutrophil absorptive capacity was characterized by a decrease between the 7th to the 20th day of bedrest, then a brief recovery, another decrease and, finally, a rise toward normal at the end of bedrest.

These changes in the absorptive capacity of leucocytes during bedrest were less pronounced in subjects who engaged in physical exercise.

The digestive function of neutrophils also undergoes substantial variation during bedrest. During the first few days of bedrest the neutrophils killed three to four times the number of bacteria compared with control values, then a progressive decrease toward normal values. The digestive capacity of neutrophils did not show a second sharp drop near the end of bedrest as was observed in the case of the absorption function.

Eleven of 12 subjects who received repeated bacteriological examinations showed a substantial increase (10 to 100 times) in the number of staphylococci that could be cultured from the nasal mucosa during bedrest. In the control period most of the cultures of staphylococci showed no signs of pathogenicity, but during bedrest the signs of pathogenicity increased. In cases in which pathogenic cultures were present in the pre-bedrest period, their pathogenicity increased substantially during bedrest. There was a considerable increase in the antienzyme antibodies during bedrest; the titer of antilecithinose increased twofold and antihyaluronidase up to eightfold.

Conclusions:

The absorptive capacity of leucocytes is stimulated early in bedrest, followed by a protracted period of suppression and subsequent tendency to recover.

During bedrest the various stages of phagocytosis do not always change simultaneously in the same direction; suppression of one stage in phagocytosis may not be accompanied by a similar change in the other stage.

The increased titer of specific staphylococus antibodies during bedrest is primarily due to an increase in the pathogenic activity of the microorganisms.

Both the nonspecific resistance to infection and the specific immunological reactivity of the body change during bedrest. This appears to result in intensified activity of conditionally pathogenic and saphrophytic automicroflora vegetating in the body and may also contribute to activation of latent infection or propagation of an agent introduced from the outside.

43. Chukhlovin, B. A., P. B. Ostroumov, and S. P. Ivanova. Development of staphylococcal infection in human subjects under the influence of some spaceflight factors. *Kosmicheskaya Biologiya i Meditsina* 5:61-65, 1971.

Authors' abstract: Healthy male test subjects exposed to extended bedrest, partial or complete isolation, and inadequate personal hygiene were studied for the size of microbial foci in the nasal mucosa and pathogenicity of nasopharyngeal staphylococci. Most test subjects exhibited an increase in size of staphylococcal foci and an increased presence of staphylococci producing coagulase, hyaluronidase, and lecithovitellase. They also exhibited an increased level of antibodies to staphylococcal enzymes in the blood. The carrying of a main phagotype was usually established in isolated groups of subjects. The possibility of mutual infection of human subjects by pathogenic staphylococci under the influence of certain spaceflight factors was demonstrated.

44. Chung, A. T.-C. Creatine, creatinine and nitrogen excretion by bedrest recumbent male subjects. Master of Science Thesis, Texas Woman's University, Denton, Texas, Aug. 1966.

Author's summary and conclusions:

Four healthy adult males participated in this study which consisted of a 29-day pre-bedrest period, a 30-day bedrest period, a 31-day post-bedrest period, and a 30-day post-post-bedrest period.

During the pre-bedrest period, the average urinary creatinine and creatine excretion values for all four subjects were within the normal range according to standards set by *Walker and Boyd (44)*. The overall average excretion of total nitrogen among all four subjects was also within the normal range of urinary nitrogen excretion.

Three of four subjects did not show any statistically significant change of urinary creatinine excretion value during bedrest as compared with both the ambulatory and recovery periods, whereas all four subjects had statistically significant rise in the urinary excretion of creatine during this period. The increase in urinary nitrogen excretion was also statistically significant for all four subjects. The excretion of creatinine for all four subjects during the two recovery periods did not show any statistically significant change when these two periods were compared with each other. During the entire recovery period, creatinine excretion for all subjects demonstrated little significance as compared with both pre-bedrest or bedrest periods.

Three of four subjects did not show any statistically significant difference in their excretion values of creatine when the post-bedrest period was compared with the post-post-bedrest period. During the entire recovery period, the excretion of urinary creatine gradually returned to normal, but still higher than the excretion during the pre-bedrest period. Three of four subjects had significantly higher levels of creatine excretion when they were compared with the excretion level of the pre-bedrest period.

Two of four subjects did not show any statistically significant change in the total nitrogen excretion during the post-post-bedrest period as compared with the excretion of the post-bedrest period. During the entire recovery period, nitrogen excretion returned to the normal excretion value. All four subjects showed statistically significant decreases in total urinary nitrogen excretion as compared with the bedrest period.

It is apparent from the findings of this study that the excretion of creatinine did not show any significant change throughout the whole study. Both creatine and nitrogen excretion increased significantly during the immobilization period. Creatine excretion and nitrogen excretion seemed to increase or decrease parallel to each other, probably because both are primary muscle substances.

45. Cooper, K. H. and J. W. Ord. Physical effects of seated and supine exercise with and without subatmospheric pressure applied to the lower body. *Aerospace Medicine* 39: 481-484, 1968.

Author's abstract: Eight subjects were evaluated on a bicycle ergometer once a week for 4 weeks in both the upright and the supine posiiton, with and without the addition of -30 mm Hg lower-body negative pressure. Upright ergometry without negative pressure was associated with the highest maximum oxygen consumption, wheras upright exercise with negative pressure and supine exercise with and without negative pressure were remarkably comparable. The cardiovascular response during submaximal upright exercise with negative pressure resembled that seen after physical deconditioning. This difference was not as apparent at maximum performance. These results indicate that in an earth environment the integration of LBNP with upright exercise provides an overload phenomenon that may be used to accelerate a cardiovascular conditioning response. In space, the mechanics of exercise might be facilitated, a good cardiovascular conditioning device could be provided, and a means of orthostatic stress testing would be available.

46. Cordonnier, J. J. and B. S. Talbot. The effect of the ingestion of sodium-acid phosphate on urinary calcium in recumbency. *Journal of Urology* 60: 316-320, 1948.

Purpose: To determine if administration of sodium-acid phosphate will reduce urinary calcium output.

Procedure and methods: In all, 71 bedridden patients were studied. Urinary calcium was measured on 24-hr urine specimens and combined for three successive days. Sodium-acid phosphate (5.8 gm daily for 10 days) was administered to 16 patients.

Results: The daily excretion of calcium in 20 ambulatory controls was 223 mg/24 hr compared with 310 mg/24 hr in the recumbent patients; both groups were eating the same general diet. In 16 patients receiving sodium-acid phosphate, the control calcium excretion averaged 366 mg/24 hr and was reduced to 189 mg/24 hr after phosphate administration. Urinary calcium was reduced in every patient.

Conclusions: Hypercalcinuria is one of the more important factors in the formation of urinary calculi in recumbency. The excretion of urinary calcium can be definitely reduced by the administration of sodium-acid phosphate.

47. Cuthbertson, D. P. CXLV. The influence of prolonged muscular rest on metabolism. *Biochemistry Journal* 23:1328-1345, 1929.

Purpose: To investigate some metabolic aspects of disuse atrophy in healthy subjects during bedrest.

Procedure and methods: Five men, 19 to 40 yr, and two women, 19 and 37 yrs, were studied. They were healthy but some had a loose cartilage in the knee joint. The subjects were confined to the ward for 5 days to reach nitrogen equilibrium. Then one lower limb was encased in a well-padded osteotomy splint, the footpiece being anchored. The subjects were propped up in bed and asked to limit all superfluous movements. Food intake was selected by the subjects and then, with water intake, was kept constant during bedrest. The subjects were confined to bed for periods between 13 and 44 days.

Author's summary: Subjects in nitrogenous equilibrium show, within a day or two from the commencement of a period of muscle rest of the order described, a rise in the excretion of sulpher, nitrogen, phosphorus, and calcium, in that order of priority. This loss is maintained fairly steadily for a varying period, after which it gradually declines. The rise in the excretion of sulphur is due to a practically proportionate increase in inorganic sulphate. Ethereal sulphate tends to decrease, while neutral sulfur remains more constant. The rise in the excretion of nitrogen is mainly due to a proportionate increase in the amount of urea. Ammonia excretion also rises, but more slowly. Creatinine and uric acid are practically unaltered.

The S:N ratio suggests a sulfur-rich source of the excreted material, presumably for the most part muscle. Apart from a slight fall in the oxygen consumption, associated with a rise in the respirator quotient, the gaseous metabolism remains very constant from day to day. Maxima and minima percentage day-to-day variations in the oxygen consumption gradually decrease as the experimental period lengthens, from ±14 to ±1.2 percent.

48. Degtyarev, V. A., A. D. Voskresenskiy, N. D. Kalmykova, and Z. A. Kirillova. Functional test with decompression of the lower body in thirty-day antiorthostatic hypokinesia. *Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina* 8:61-65, 1974.

Authors' abstract: During a 30-day hypokinetic experiment, nine test subjects underwent functional tests with LBNP applied at −35 and −45 mm Hg for 10 min. Subjectively, they tolerated the tests well. Cardiovascular responses were similar to orthostatic responses but less pronounced. During hypokinesia the response to the tests increased. A statistical analysis of the relationship between the heart rate and integral evaluations revealed a correlation between responses to LBNP of −45 mm Hg and the orthostatic load ($r = 0.71$). This indicates the possibility of predicting orthostatic reactions on the basis of LBNP tests.

49. Deitrick, J. E., G. D. Whedon, E. Shorr, V. Toscani, and V. B. Davis. Effects of immobilization upon various metabolic and physiologic functions of normal men. *American Journal of Medicine* 4:3-35, 1948.

Purpose: To investigate the metabolic and physiologic effects of immobilization on normal, healthy young men and to furnish a basis for differentiating the effects of immobilization per se from those which might arise from disease or trauma.

Procedure and methods: Four normal, healthy male conscientious objectors (20 to 29 yr) underwent an ambulatory control period (6 to 8 weeks) where they underwent ½ hr of calisthenics and ½ hr of swimming each day; a bedrest period (6 weeks in the first pair of subjects and 7 weeks in the second pair) while immobilized in plaster casts encasing the pelvic girdle and legs; and a recovery period (4 weeks in the first pair and 6 weeks in the second pair).

The subjects ate a controlled diet of 2500 kcal for one subject and 2800 kcal for the other three subjects. The 2800-kcal diet was composed of 16 percent protein (90 gm), 63 percent carbohydrate (352 gm), and 20 percent fat (114 gm). Calcium, phosphorus, and potassium were kept constant at 0.92 gm/day, 1.64 gm/day, and 3.76 gm/day, respectively, for the 2800-kcal diet. Sodium intake was not controlled in the first pair of subjects but it was controlled at 4 gm/day in the second pair.

Authors' summary: A study of the effects of immobilization upon various metabolic and physiologic functions of four normal, healthy young men was carried out on a metabolism ward during control (5 to 7 weeks), immobilization (6 to 7 weeks), and recovery (4 to 6 weeks) periods. Throughout the study, dietary intake was kept constant. During the immobilization period the subjects were placed in bivalved plaster casts extending from the umbilicus to the toes.

Nitrogen excretion began to increase on the fifth to sixth day of immobilization and reached its peak during the first half of the second week. Total nitrogen losses ranged from 29.8 to 83.6 gm and averaged 53.6 gm.

Both urinary and fecal calcium excretion increased during immobilization, maximum excretion being reached by the fourth to fifth week. Total calcium losses ranged form 9 to 23.9 gm. The calcium content of the urine doubled during immobilization. The absence of appreciable increase in urine volume,the slight rise in urinary pH, and the failure of urinary citric acid to rise parallel with the increase in calcium would all favor the precipitation of calcium phosphate in the urinary tract. A slight elevation in serum calcium levels occurred at the end of the immobilization period.

During immobilization there was an increase in the excretion of phosphorus, total sulfur, sodium, and potassium. Total sulfur was excreted in the urine in close correlation from week to week with urinary nitrogen in the ratio in which these elements exist in muscle protoplasm. The changes in phosphorus excretion showed moderately good correlation with the changes in nitrogen and calcium excretion.

During recovery there was retention of nitrogen, calcium, phosphorus, sulfur, and potassium. The recovery or return to control levels of metabolic functions was slow, retention of nitrogen and phosphorus continuing for 6 weeks. Restabilization of calcium metabolism appeared to require more than 6 weeks.

Although creatine and creatinine excretion remained fairly constant, there was a definite lowering of creatine tolerance during immobilization. This impairment in creatine metabolism was accompanied by a significant decrease in muscle mass and muscle strength in the immobilized limbs.

In only one subject was there a significant lowering of 17-ketosteroid excretion during immobilization; this subject also experienced the largest nitrogen losses.

The decline in basal metabolic rate during immobilization averaged 6.9 percent among the four subjects.

Immobilization brought about a deterioration in the mechanisms essential for adequate circulation in the erect position as indicated by an increased tendency to faint in tilt-table tests. Experiments indicated that the legs were the principal site of changes responsible for this deterioration and suggested that increased venous engorgement, increased extravascular fluid, capillary fragility, and impaired venous or muscle tone play a role.

Other circulatory changes brought about by immobilization were a decline in total blood volume averaging 5.4 percent, marked decreases in exercise tolerance as measured by Master and Schneider tests, and an increase in the resting pulse rate of 3.8 beats/min during immobilization, followed by an additional increase of 4.7 beats/min during the first 3 weeks of recovery.

The recovery or return to control levels of most physiologic functions required 3 to 4 weeks; exercise tolerance and leg girth required 4 to 6 weeks and the reclining pulse rate more than 6 weeks.

Changes in body weight during immobilization were small, probably as a result of the simultaneous loss of muscle protoplasm and storage of fat or carbohydrate.

There were no significant changes due to immobilization in blood coagulation studies, blood circulation time, heart size, electrocardiograms, resting arterial blood pressure, hematocrits, blood counts, vital capacity, maximum ventilation capacity, or breath-holding.

50. Dick, J. M. Objective determinations of bone calcium levels. *Aerospace Medicine* 37:136-139, 1966.

Author's summary: Calcium losses in the urine and bone matrices were determined during a 2-week period of simulated weightlessness for eight subjects. The urine was chemically analyzed and the wedge-densitometer technique was utilized in making the bone determinations. The only rigid restraint placed on the subjects was that of remaining in a horizontal plane. Movement in the horizontal plane was permitted.

Within the scope of this experiment, the following conclusions are stated: The wedge-densitometry technique of measuring bone calcium loss is practical and demonstrates a much greater ability (20 to 30 times) to determine bone density changes than the conventional subjective techniques now available. Analytically speaking, the wedge-densitometer technique is sound.

The amount of calcium loss to be expected is of a low magnitude if the physical condition of the subject is maintained. For a 30-day period, no loss in skeletal structural rigidity will be incurred. With proper

weight. Supplemental PO4 prevented the increased urinary Ca excretion which accompanies BR but had no consistent effect on fecal Ca; the negative Ca balance appeared to be attenuated but calcaneal mineral loss was not diminished.

55. Donaldson, C. L., S. B. Hulley, J. M. Vogel, R. S. Hattner, J. H. Bayers, and D. E. McMillan. Effect of prolonged bedrest on bone mineral. *Metabolism* 19: 1071-1084, 1970.

Authors' abstract: Three healthy adult males were restricted to complete bedrest for periods of 30-36 weeks. Urinary calcium excretion was elevated throughout bedrest, averaging 61 mg/day above the baseline value of 193 mg/day. Maximum urine calcium excretion occurred during the seventh week and was 136 mg/day above the baseline value. Fecal calcium excretion was also increased during bedrest. Sweat calcium was unchanged and represented only 2 percent of calcium output. Mean calcium balances for the three subjects during bedrest were −202, −207, and −254 mg/day. The measured calcium loss during the entire bedrest period averaged 4.2 percent of the estimated total body calcium. Calcium balance became more normal but remained negative during the 3-week period of reambulation. Phosphorus excreted in the urine and phosphorus balance patterns were similar to calcium patterns. Serum calcium and phosphorus levels did not change appreciably during bedrest, but both levels fell during reambulation. Urinary hydroxyproline and pyrophosphate were mildly elevated during bedrest and fell with reambulation. Gamma-ray transmission scanning of the os calcis revealed large losses of mineral during bedrest. The decreased mass in the central portion of this bone ranged from 25 to 45 percent. Mineral reaccummulated in the central os calcis following reambulation at a rate similar to its rate of loss during bedrest. Bone dissolution during bedrest may occur to a greater extent in weight-bearing bones than in the remainder of the skeleton, and the process appears to be reversible.

56. Dorokhova, Ye. I. Coagulability of blood during prolonged hypodynamia according to thromboelastographic data. *Problemy Kosmicheskoy Biologii* 13:108-112, 1969.

Purpose: To study blood coagulation during bedrest.

Procedures and methods:

Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest.

Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of air cuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt-table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Measures of blood coagulation were made with the thromboelastogram (TEG), the Poller heparin tolerance of the plasma, the Howell plasma recalcification time, the Rutberg fibrinogen content, the Tugolukov prothrombin index, fibrinolytic activity, and clot retraction.

Results: Prolonged bedrest is accompanied by the appearance of a general hemophylic response. Physical exercise on a treadmill reduces the hemophilic shifts during bedrest. Occlusion conditioning tends to offset the thrombophilic effect of the physical exercise. The blood-clotting indicators were closer to those observed in pure hypodynamia in the subjects who received occlusion conditioning than in subjects who engaged only in physical conditioning.

57. Drozdova, N. T. and Ye. P. Grishin. State of the visual analyzer under hypokinetic conditions. *Komicheskaya Biologiya i Meditsina* 6:46-49, 1972. (same study as Balakhovskiy *et al.*, 1972).

Purpose: To investigate selected visual functions and retinal blood circulation in man during 30 days bedrest.

Procedure and methods: Nine healthy men, 20 to 37 yr, were subjected to bedrest for 30 days, and their beds were tilted head downward 4° from the horizontal. The subjects were divided into three groups of three subjects each: group 1 (daily isotonic exercise (500 kcal/day) for 24 days, then, in addition to the exercise, lower body negative pressure on days 26 through 30), group 2 (no exercise control), and group 3 (isometric exercise by electrical stimulation of the muscles). Visual function was measured by ophthalmoscopic, photocalibrometric, and ophthalmodynamometric methods. Visual acuity, both near and far, and the near point of clear vision were measured.

Results: Prior to bedrest, all visual measurements were normal. After 5 days of bedrest, near point visual acuity was decreased 23 percent in group 1, −15 percent in group 2, and −20 percent in group 3. The closest point of clear vision for all subjects was moved away by an average of 2 cm, but it did not change for one subject in group 1. Upon examination of the frontal segment of the eyes, edema of the eyelids (greater for the lower ones), a strengthening of the vascular pattern, and hyperemia of the conjunctiva was observed. Ophthalmoscopic examination revealed a pronounced dilation of the retinal vessels, particularly the veins. The background of the ocular fundus appeared darker and the boundaries of the optic nerve disk were irregular and small vessels could be seen.

Photocalibrometry revealed an increase in the lumen of the retinal vessels. The diameter of the retinal arteries increased 22 percent and the veins increased 29.3 percent in group 1; the respective increases in group 2 were 26 and 35 percent and, for group 3, 32 and 48 percent.

Diastolic pressure in the central artery in group 1 increased 22 percent, increased 8 percent in group 2, and increased 15 percent in group 3.

These changes mentioned above persisted on the 11th, 20th, and 29th days of bedrest. On the 4th day of recovery, the closeup visual acuity for groups 2 and 3 remained impaired while that for group 1 showed some improvement. Most changes that occurred during bedrest returned to normal by the 10th day of recovery. The only exception was that the diastolic pressure in the retinal artery remained elevated in group 1.

Authors' conclusions: Enlargement of the diameter of the retinal arteries is apparently the result of a decrease in vascular tone and a decrease in the mass of circulating blood. Dilatation of the small vessels can probably be regarded as a compensatory reaction for improvement of blood flow to the retinal nerve cells. The decrease in visual acuity (both closeup and distant) and the increase in distance of the closest point of clear vision can be attributed to a decrease in the functioning of the muscular apparatus of the eye and also, in part, to the general hypoxia prevailing at this time. It was concluded that 30 days of bedrest causes some adverse changes in ocular hemodynamics and visual functions. The changes were more pronounced in the no exercise group compared with the two other groups that had either isometric or isotonic exercise. Normal visual function was restored when the subjects shifted to the upright ambulatory posture.

58. Drozdova, N. T., and O. N. Nesterenko. State of visual analyzer during hypodynamia. *Problemy Kosmicheskoy Biologii* 13:189-191, 1969.

Purpose: to investigate visual function during 70 days bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M, M-k, V, M-k) were given treadmill exercise with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercise on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercise on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt-table during weeks 3-4 and 7-8. Before centrifugation these subjects were give drugs.

Measurements of visual function were made before bedrest, on days 45 and 67 of bedrest, and on the 2nd and 20th day out of bed in recovery. Before and after bedrest the subjects were subjected to transverse ($+G_X$) acceleration (intensity and duration not indicated).

Results:

In the control period, visual acuity averaged 1.25, peripheral vision extended to 62.3° intraocular pressure averaged 20 mm Hg, the near point of clear vision was at 8.5 cm, the area of the blind spot was 75 cm^2 (determined at a distance of 1 m with a 0.5-cm white object), and the recovery time of visual acuity (after an exposure to 900 nits for 3 min) was 27 sec. The ocular fundus picture was normal for all subjects: the optic disk was pale pink with peculiarities of blood-vessel size. The only deviations from normal was a decrease in visual acuity to 0.4 in one eye in subjects Ch-y and M-s and to 0.9 for subject G-y.

After 45 days of bedrest compared with control values, visual acuity had decreased by an average of 21 percent, peripheral vision was 11° narrower, intraocular pressure decreased 3 mm Hg, and the near point was consistently more distant by an average of 3.5 cm.

After 67 days of bedrest compared with control values, peripheral vision had narrowed 15° and the near point had moved out an average of 12.5 cm.

On the second recovery day compared with control values, average visual acuity remained depressed by 21 percent, the blind spot was enlarged 38 percent, and the time to recover visual acuity after the light flash was increased 120 percent. The fundus showed fading of the optic disk and its temporal boundary was somewhat indistinct. The veins had enlarged, were distended, and darker in color. There was moderate enlargement of the retinal arteries.

On the 20th recovery day compared with control values, visual acuity was still decreased 19 percent, the visual recovery time was still 50 percent longer than control values, the reactive vascular effects had receded, the arteries had returned to their normal size, the veins were only slightly enlarged, and the optic disk was pink with sharp outlines. There were no changes in field and color perception during 70 days of bedrest.

During centrifugation before bedrest, the veins and arteries of the fundus were enlarged, the background of the retina was red, and the boundaries of the optic disk were sharp after the subjects had sustained the maximal permissible accelerations. The vascular reactions were most pronounced in the group I (control) subjects following $+G_X$: the minute vessels on the optic disk were visible and the retinal background was bright red. In group II (drugs), there was a sharp constriction of the retinal arteries while the veins remained of normal size. In group III (physical exercise), the reactive vascular effects were less pronounced: the arteries were slightly enlarged and the veins moderately dilated and tensed. In groups IV and V, the reactive vascular changes were mild: the arteries were dilated slightly and the veins moderately.

Conclusions: Prolonged bedrest induces adverse changes in the functioning of the eye, but the changes are not so profound as to disable the visual apparatus. Resumption of motor activity results in progressive recovery of the disturbed functions, but recovery is not complete 20 days after bedrest. The changes in visual function appear to be due to retinal hypoxia consequent to changes in intracranial blood flow.

59. Eichelberger, L., M. Roma, and P. V. Moulder. Effects of immobilization atrophy on the histochemical characterization of skeletal muscle. *Journal of Applied Physiology* 12:42-50, 1958.

Authors' abstract: Experimental immobilization of one hind leg of puppies was produced to study biochemical changes in immobilization atrophy in the calf and thigh groups of muscles. The opposite leg or the sound one was used as the control leg. The puppies were arranged into three groups according to age and duration of immobilization: group I, 12-14 weeks of age with 4-5 weeks of immobilization; group II, 13-17 weeks of age with 6-7 weeks of immobilization; and group III, 17-20 weeks of age with 8-11 weeks of immobilization. An important finding in the original data was the progressive increase in total neutral fat content, depending on the length of time of immobilization. The histochemical patterns for 1 kg of these muscles have been considered and control values compared with atrophic values. Irrespective of age or duration of immobilization, there were increases in the extracellular compartment mass, which were the result mainly of an increased water content in this phase. The increased extracellular water was at the expense of the intracellular water. Simultaneous with the decrease in intracellular water content was a decrease in the solid mass of this phase to such an extent that the percentage of intracellular water in the atrophied muscle was the same as that in the sound muscle. Using the histochemical patterns for 1 kg of muscle, evidence has been presented to show that the internal structure of the muscle fibers did not change in immobilization atrophy. In all three groups of puppies, the percentage of muscle fiber water, as well as the potassium and magnesium concentrations, was the same whether expressed per kilogram of muscle fibers or per kilogram of muscle fiber water in all the calf and thigh groups of muscles from both the control and immobilized legs.

60. Ellis, J. P., Jr., F. R. Lecocq, J. B. Garcia, Jr., and R. L. Lipman. Forearm amino acid metabolism during chronic physical inactivity. *Aerospace Medicine* 45:15-18, 1974.

Authors' abstract: The effect of 14 days of physical inactivity on peripheral amino acid metabolism was determined on a group of five healthy male subjects ranging in age from 18 to 20 yr. Blood samples were drawn from the right brachial artery and a left brachial vein during the control period of 2 weeks and on the 14th day of bedrest. None of the 19 amino acids analyzed showed a significant change, either in uptake or release, from the forearm muscles. However, a substantially higher level of alanine was found in both arterial and venous blood of the physically deconditioned subjects. As the forearm retains considerable activity during bedrest, it was suggested that the higher level of alanine in arterial blood probably originated from more gravity-dependent muscles and that the observed higher venous level of alanine was a passive consequence of the corresponding arterial level.

61. Ellis, J. P., Jr., B. E. Welch, and J. M. Prescott. Effects of hypercapnia and physical deconditioning on musculoskeletal protein in man. *Aerospace Medicine* 43:22-27, 1972.

Authors' abstract: A recently developed automated chromatographic method for quantifying urinary peptides and free amino acids was used to ascertain the effects of confinement, physical deconditioning, and hypercapnia on a group of three healthy male subjects. A 4-day control period preceded a 15-day experimental period, during which time the subjects were housed in a small airtight environmental chamber. The chamber air was the same as room air, except for the middle third of the experiment during which time it was adjusted to contain 3 percent CO_2. The following urinary excretion trends were found: (a) a generalized reduction in amino acids and aminopeptides, (b) a sharp rise, followed by an abrupt fall, in one hydroxyproline peptide, and (c) a less marked but progressive increase in another hydroxyproline peptide. The timing and magnitude of the latter two changes suggest that perhaps two types of body collagen may have been partially degraded by confinement and/or deconditioning.

62. Epstein, M. Effect of prolonged bedrest on renal diluting capacity in normal man. *Journal of Applied Physiology* 30:366-369, 1971.

Authors' abstract: The effects of 2 weeks of absolute bedrest on renal diluting capacity were studied in eight normal young male subjects. An acute sustained oral water load of 20 ml/kg was administered during a control period of normal activity, on the 13th day of absolute bedrest, and on the 4th or 14th day of post-bedrest recovery. Bedrest did not significantly alter peak urine flow corrected for GFR (V/GFR), ability to generate free water (C_{H_2O}), or to achieve minimal urine osmolality. The results suggest that despite analogies with adrenal insufficiency, including both a decrease in plasma volume and a decrease in adrenocortical reserve, prolonged bedrest does not impair renal diluting capacity.

63. Fasola, A. F. and J. H. Triebwasser. The renin response to lower body negative pressure stress testing and the effect of exercise during prolonged bedrest. Aerospace Medical Association Preprints, 1970, pp. 63-64.

Purpose: To determine the renin response to lower body negative pressure and the effect of exercise during prolonged bedrest.

Procedure and methods: Eight healthy volunteers from 18-22 yr, were subjected to 5 weeks of control, 5 weeks of bedrest, and 6 weeks of recovery. Each subject expended 600 kcal of energy per day during the control and recovery phases. During the bedrest phase, four of the eight subjects continued to exercise while the remaining four were placed on strict bedrest. Each volunteer was subjected to lower body negative pressure (LBNP) of 40 mm Hg for 20 min during the first, third, and fifth weeks of control; 30th day of bedrest; 48 hr, 2, 4, and 6 weeks after immobilization. Blood was drawn before and during the 19th min of LBNP exposure to determine renin activity.

Results: There was no significant difference in renin activity between exercisers and nonexercisers during the control period. During the fifth week of bedrest, the baseline renin activity increased in both groups but to a greater degree in the nonexercising group. The renin activity in both groups returned to approximately control levels during the fourth week of recovery. All subjects showed a significant increase in renin activity following exposure to LBNP during control, bedrest, and recovery. The nonexercising subjects had a greater increment increase in renin activity after LBNP exposure compared to the exercising group.

Conclusions: It appears from the results that plasma renin activity is increased as a result of strict bedrest and that the effects of bedrest were attenuated by exercise. It is also apparent that weightlessness, as simulated by strict bedrest, does not remove the stimulus for renin release and that the renin-angiotensin system is reset at a higher than normal level.

64. Filatova, L. M. and O. D. Anashkin. Changes in the human blood clotting system caused by prolonged hypokinesia. *Byulleten' Eksperimental'noi Biologii i Meditsiny* 65:36-38, 1968. (Same study as: Cherepakhin 1968a, Cherepakhin 1968b, Georgiyevskiy, et al. 1968, Kakurin 1968, Petukhov et al. 1968).

Purpose: To investigate the effect of physical exercise on the changes in the blood clotting system during bedrest.

Procedure and methods: Six healthy men (24 to 36 yr) were confined to bed for 62 days. Group A consisted of three men who performed a series of isometric and isotonic exercises for 2-1/2 hr/day in the horizontal position (see Cherepakhin 1968a for a complete description of the exercises used). Group B (three men) served as non exercise controls.

Venous blood samples were collected before and on days 8, 28, 46, and 56 during bedrest. Measurements made were plasma heparin tolerance, plasma recalcification time, thromboplastin time and activity of the prothrombin complex, proaccelerin concentration, thrombin time, fibrinogen concentration, fibrinolytic activity, platelet resistance, thromboelastrography, and the tourniquet test.

Results: The changes in the blood clotting system were found to be cyclic in character.

In all six subjects on the eighth day of bedrest, (a) activity of the procoagulants was increased as indicated by a significant shortening of the thromboplastin time, (b) there was an increase in activity of the prothrombin complex, (c) a mean increase in proaccelerin of 15.5 percent, (d) an increase in fibrinolytic activity of 23.5 percent, (e) a 10-percent increase in plasma heparin tolerance, (f) an average shortening of the recalcification time by 17 percent, and (g) the platelet resistance increased by 3.7 times.

On the subsequent days of bedrest, the differences between the subjects were inconsistent, regardless of whether they exercised or not. In two subjects (one exerciser and one nonexerciser), the increased procoagulant activity observed in both subjects on the eighth day was still present, but on the thromboelastogram R was shortened by 29 percent and K by 55 percent, plasma heparin tolerance was increased by 37 percent, the recalcification time shortened by 17 percent, the platelet resistance increased by 32.5 percent, fibrinogen concentration was reduced by 33 percent, and the fibrinolytic activity was increased by 40 percent.

In four subjects (two exercisers and two nonexercisers), the blood changes were different in character. On the 27th day of bedrest, the clotting power of the blood had fallen to a minimum with a lengthening of the plasma recalcification time by 36 percent, an increase in thromboplastin time of 15 percent, a decrease in prothrombin activity of 13 percent, a decrease in fibrinogen concentration of 22 percent, and an increase in fibrinolytic activity of 56 percent. The other indices likewise indicated diminished clotting power: the thromboelastogram R was lengthened by 32 percent and the K by 26 percent, the plasma heparin tolerance was reduced by 83 percent, the thrombin time was increased by 12.5 percent and the platelet resistance was reduced by 10 percent. With slight fluctuations these changes persisted throughout the period of bedrest, except for the fibrinogen concentration which fell to a minimum on the 28th day, increased by 11 percent on the 46th day, and increased by 14 percent on the 56th day.

Conclusions: During bedrest the increase in fibrinogen concentration appears to be a protective reaction by the body to the increase in fibrinolytic activity manifested by the increased synthesis of fibrinogen in the liver cells. The increased clotting power of the blood observed on the 8th day of bedrest may be explained by a generalized stress reaction of the body to the constraints imposed by putting healthy subjects to bed. However, the increase in the level of blood procoagulants, with the possibility of thrombosis, was not sufficient to cause intravascular clotting of the blood. For clotting to occur, a depression of the physiological anticlotting system or a disturbance of the integrity of the blood vessel wall is necessary.

The first days of confinement to bed are the most dangerous in regard to venous and arterial thrombi. The most highly developed protective measure against thrombosis was the increase in fibrinolytic activity, which had risen by 20 to 33 percent by the eighth day of bedrest.

The physical exercise did not ameliorate the changes in the blood-clotting system induced by the bedrest.

It is postulated that the increased fibrinolytic activity during bedrest may be triggered by the release of plasmokinase from the endothelium of the blood vessels (arterioles) induced by a change in arteriolor tone.

65. Fuller, J. H., E. M. Bernauer, and W. C. Adams. Renal function, water and electrolyte exchange during bed rest with daily exercise. *Aerospace Medicine* 41:60-72, 1970 (From Bernauer, E. M. and W. C. Adams. The effect of nine days of recumbency, with and without exercise, on the redistribution of body fluids and electrolytes, renal function and metabolism. NASA CR-73664, 1968).

Authors' abstract: Eight young adult males underwent 9 days of continuous recumbency, during which half exercised 30 min twice daily on a horizontal bicycle ergometer, while the remainder served as controls. Ten days before and during bedrest, metabolic exchange of water, sodium, potassium, and chloride was calculated; 7 days following bedrest, water and electrolyte input was ad libitum and output was measured. P-amino hippurate (PAH) and creatinine clearances in resting and exercise states and blood volume were measured during all three periods, while lean body mass (LBM), body fat, and total body potassium were measured before and after bedrest. On the first day of recumbency, urinary volumes were increased by 11 and 18 percent, sodium balance was −71 and −109 mEq, and chloride balance was −61 and −74 mEq in the exercise and control groups, respectively. Thereafter, these parameters were slightly increased, whereas potassium excretion remained elevated throughout bedrest, with a cumulative loss of 80 mEq in the exercise and 174 mEq in the control group. Renal clearance of PAH increased 250 ml/min, creatinine increased 11 ml/min, and plasma volume decreased 7 percent relative to pre-bedrest values in the control group, whereas these parameters changed only slightly in the exercise group. Loss of LBM and total body potassium and gain of body fat was two to three times greater in the controls. Although body water, sodium, chloride, and blood volume seemed to be reset initially at lower levels during recumbency and after several days were less affected, while other parameters appeared to change according to the length of bedrest, and were better stabilized when exercise was employed.

66. Genin, A. M. and L. I. Kakurin. Thirty-day experiment with simulation of the physiological effects of weightlessness. *Kosmicheskaya Biologiya i Meditsina* 6:26-28, 1972.

Purpose: To give the overview of the 30-day-bedrest project described in more detail in the papers by Drozdova et al., 1972; Pestov et al., 1972; Yarullin et al., 1972; Balakhoskiy et al., 1972; Stepantsov et al., 1972; Katkovskiy et al., 1972; Pometov et al., 1972; Voskresenskiy et al., 1972; An effort was made to evaluate the compatibility of different remedial procedures to alleviate bedrest deconditioning and their effect on orthostatic tolerance. The remedial procedures tested were walking on a vertical treadmill, lower body negative pressure, and electric stimulation of the muscles (isometric exercise).

Procedures and methods: See the paper by Voskresenskiy et al., 1972.

Conclusions: The use of the hypodynamic model in which the subjects are positioned with their head angled downward 4° from the horizontal (antiorthostatic position) introduces some new elements into the picture, that is, increased blood flow to the head and the illusion of tumbling when the eyes are closed.

67. Genin, A. M. and P. A. Sorokin. Prolonged limitation of mobility as a model of the influence of weightlessness on the human organism. *Problemy Kosmicheskoy Biologii* 13:9-16, 1969.

Authors' abstract: This paper examines experimental approaches to evaluation of the biological effects of prolonged weightlessness. Laboratory simulation of weightlessness, with prolonged bedrest as an example, is defended. The initial conception that formed the basis for the 70-day hypodynamia study is formulated.

68. Genin, A. M., P. A. Sorokin, G. I. Gurvich, T. T. Dzhamgarov, A. G. Panov, I. I. Ivanov, and I. D. Pestov. Basic results from studies of the influence of 70-day hypodynamia on the human organism. *Problemy Kosmicheskoy Biologii* 13:248-253, 1969.

Purpose: To generalize on the experimental data obtained from the Soviet 70-day-bedrest study and to point out possible cause-and-effect relationships. The following questions were studied: (a) the mechanism of the shifts resulting from prolonged bedrest on mobility when restricted to the horizontal position, (b) the mechanism by which these shifts arise during bedrest, and (c) the possibility of mitigating the adverse effects of prolonged bedrest by the use of drugs, physical exercise, and two different prophylactic complexes that included drugs, occlusion cuffs, and two varieties of physical conditioning.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cycle basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results: Expected consequences of prolonged confinement to bed:

Primary reactions: (1.) hypodynamia due to reduced gravitational load on supporting structures and restriction of mobility, (2.) lowered hydrostatic pressure of blood and absence of hydrostaticpressure fluctuations in vessels, and (3.) changes in activity of afferent systems.

Mediated reactions: (1.) absence of static tension of postural musculature, (2.) lowered energy metabolism, (3.) negative nitrogen balance, (4.) atrophy of muscles, reduction of muscular mass, decreased strength, and endurance, (5.) decrease in body weight at expense of muscle component, (6.) decalcification of bones, (7.) excretion of creatinine with urine, (8.) loss of motor habits, (9.) deconditioning of cardiovascular system, (10.) redistribution of blood toward thorax, (11.) increased diuresis, (12.) plasma loss and lowered circulating-blood volume, (13.) decrease in body weight due to dehydration, (14.) deconditioning of cardiovascular system with respect to hydrostatic factor, (15.) lowering of interoceptive afferentation including that from vascular-bed receptors, (16.) change in proprioceptive afferentation (muscle-joint sensation), (17.) psychological stress, (18.) disturbed sleep, (19.) readjustment of reflex regulation of vegetative and somatic functions, and (20.) change in humoral regulatory link.

Resultant effects: (1) Change in physical efficiency and movement coordination, (2) lowered tolerance of transverse g forces, and (3) lower orthostatic stability.

Authors' summary: The results obtained in the course of the experiment are examined in juxtaposition to the expected consequences of hypodynamia, which are presented in diagram form.

Certain new aspects of the influence of prolonged bedrest on the organism were brought to light during the study: a decrease in immunological resistance, certain disturbances to the mental functions, the development of trophic changes in the myocardium, changes in reactivity to medication, etc. The specifically designed physical-conditioning procedures were found to be relatively most effective in mitigating the detrimental effect of hypodynamia.

69. Georgiyevskiy, V. A., V. A. Gornago, L. Ya. Divina, N. D. Kalmykova, V. M. Mikhaylov, V. I. Plakhatnyuk, Yu. D. Pometov, V. V. Smyshlyayeva, N. D. Vikharev, and B. S. Katkovskiy. Orthostatic stability in an experiment with 30-day hypodynamia. *Kosmicheskaya Biologiya i Meditsina* 7:61-68, 1973.

Authors' abstract: Nine test subjects were kept for 30 days in bed with their heads tilted 4° downward. At the end of the experiment they exhibited a decrease in orthostatic stability. The use of different countermeasures, including physical exercises and lower body negative pressure (LBNP), considerably improved their orthostatic stability. Electric stimulation of the muscles also produced a preventive effect, although to a lesser extent. It should be expected that a combination of physical exercises, LBNP, and electric stimulation of the muscles during prolonged spaceflight may exert a positive effect on orthostatic stability.

70. Georgiyevskiy, V. S., L. I. Kakurin, B. S. Katkovskii, and Yu. A. Senkevich. Maximum oxygen consumption and functional state of the circulation in simulated zero gravity. *The Oxygen Regime of the Organism and its Regulation,* edited by N. V. Lauer and A. Z. Kolchinskaya. Kiev: Naukova Dumka, 1966, pp. 181-184.

Purpose: To elucidate the effects of prolonged bedrest on maximal working capacity.

Procedure and methods: Four healthy men (22 to 25 yr) underwent bedrest for 20 days. Work tests involving increasing physical loads were performed before and after bedrest on a bicycle ergometer to the point of exhaustion.

Results: The 20-day stay in bed reduced the physical working capacity of all subjects. Before bedrest the average work performance was 5316 kg/m and only 3933 kg/m 2 to 3 days after bedrest. Three subjects had returned to normal values 8 days after bedrest. Maximal oxygen uptake averaged 3.14 liter/min before bedrest, 2.87 liter/min 2 to 3 days in recovery, and also 2.87 liter/min after 8 days of recovery. After 8 days of recovery, no subject regained his control level of maximal oxygen uptake.

After bedrest the stroke volume during exercise decreased to 86 ml from 91 ml in the control period.

For the same amount of work the heart rate during exercise was greater after bedrest (175 beats/min) compared to 158 beats/min before bedrest. Maximal pulse rate was 173 beats/min in control and 181 beats/min in recovery.

Conclusions: The fact that the subjects stopped working at almost identical values of circulatory minute volume suggests that the decrease in the amount of work performed after bedrest was dependent on circulatory function.

The attainment of identical levels of circulatory minute volume after bedrest was due to increased heart rate with decreased stroke volume, indicating a less economical mode of cardiac activity.

Decreased maximal oxygen uptake at essentially constant circulatory minute volume suggests deterioration in oxygen utilization by the tissues.

71. Georgiyevskiy, V. S. and B. M. Mikhaylov. Effect of hypokinesia on human circulation. *Kosmicheskaya Biologiya i Meditsina* 2:48-51, 1968. (Same study at Petukhov *et al.*, 1968; Kakurin, 1968; Cherepakhin, 1968a; and Cherepakhin, 1968b.)

Purpose: To investigate the combined effects of bedrest and centrifugation on various circulatory measurements.

Procedure and methods: Two series of experiments were conducted: the first, 20 days and the second, 62 days of bedrest. In each series the subjects were three healthy men (22 to 36 yr), six subjects total. The subjects were rotated on a centrifuge, subjected to bedrest with no remedial procedures, and again rotated on the centrifuge (particulars not specified). Periodically before, during, and after bedrest, circulatory function was evaluated by the techniques of mechanocardiography, polycardiography, and a 77°, head-up tilt-table test.

Summary: During bedrest there was a progressive increase in resting heart rate up to 10 beats/min during the 20-day test and up to 37 beats/min during the 62-day test. The ejection period of the heart decreased from 0.27 to 0.24 sec and mechanical systole from 0.34 to 0.30 sec. Mean arterial blood pressure and pulse pressures increased from 86 and 33 mm Hg to 97 and 39 mm Hg, respectively, at the end of the 62-day-bedrest period.

Conclusions: As a result of exposure to 20 and 62 days of bedrest, the contractability of the myocardium is not impaired, but there is an impairment in arterial vasomotor tone. The capacity for regulation is retained but impaired.

72. Gilbert, C. A., L. A. Bricker, W. T. Springfield, Jr., P. M. Stevens, and B. H. Warren. Sodium and water excretion and renal hemodynamics during lower body negative pressure. *Journal of Applied Phsiology* 21:1699-1704, 1966.

Authors' abstract: Zero-gravity conditions such as occur in orbital space flight are known to produce significant losses of body fluid and electrolyte. Lower body negative pressure (LBNP) applied to the supine subject has been suggested as a possible preventive measure. The present study demonstrated that 60 mm Hg LBNP applied for 1 hr produced moderate declines in glomerular filtration rate, renal plasma flow, and tubular reabsorption of sodium, with marked falls in rate of urine flow, free-water clearance, and sodium excretion. Although antidiuretic hormone and salt-retaining hormones may have played a role in the responses seen, the changes which occurred in sodium and water excretion appear explainable primarily on the basis of diminished glomerular filtration rate. It is concluded that LBNP is a potent stimulus to retention of salt and water and therefore has a potentially valuable place in maintaining or restoring plasma volume during prolonged weightlessness.

73. Goldmsith, R. S., P. Killian, S. H. Ingbar, and D. E. Bass. Effect of phosphate supplementation during immobilization of normal men. *Metabolism* 18:349-368, 1969.

Authors' abstract: The effect of oral inorganic phosphate supplements (1 to 2 gm phosphate-phosphorus daily) on calcium metabolism during immobilization was assessed in six healthy volunteer subjects who were placed in plaster spica body casts for 40 days. Compared to values during the control phase, those subjects who did not receive phosphate supplements showed an increased urinary excretion of calcium, negative calcium balance (averaging −152 mg/day/subject), and calcium oxalate crystalluria. In contrast, subjects who received the phosphate supplement showed a decreased urinary excretion of calcium, a lesser degree of negative calcium balance (mean −78 mg/day/subject), and no crystalluria. In addition, the hypercalciuria and crystalluria which occurred in subjects who initially did not receive a phosphate supplement were reversed when the supplement was begun. The data suggest that phosphate supplements can prevent or ameliorate the hypercalciuria, crystalluria, and negative calcium balance associated with immobilization.

74. Goodall, McC., M. McCally, and D. E. Graveline. Urinary adrenaline and noradrenaline response to simulated weightless state. *American Journal of Physiology* 206:431-436, 1964.

Authors' abstract: Sixteen normal subjects were placed in a simulated weightless state, that is, water immersion. After 6 hr of water immersion, urine samples were collected and bioassayed for adrenaline and noradrenaline. The excretion of adrenaline was moderately increased ($P < 0.15 > 0.10$), possibly related to the anxiety associated with the immersion. The excretion of noradrenaline was significantly ($P < 0.01$) reduced during immersion. Six subjects were also studied during passive vertical tilt following the immersion. The increase in pulse rate and decrease in pulse pressure were significantly greater than those observed during a control tilt. The results of these experiments indicate that the decrease in orthostatic tolerance following a simulated weightless state is probably related to a decrease in sympathetic nerve activity which, in turn, is reflected by a decline in the urinary output of the sympathetic neurohormone noradrenaline.

75. Greenleaf, J. E., W. van Beaumont, E. M. Bernauer, R. F. Haines, H. Sandler, R. W. Staley, H. L. Young, and J. W. Yusken. Effects of rehydration on +Gz tolerance after 14-days bedrest. *Aerospace Medicine* 44:715-722, 1973.

Authors' abstract: To determine if rehydration increases +Gz tolerance following bedrest deconditioning, eight male volunteers (21-23 yr) were subjected to acceleration levels of 2.1 G (740 sec), 3.2 G (327 sec), and 3.8 G (312 sec) presented in random order; the rate of acceleration was 1.8 G/min. Acceleration tolerance was determined by either loss of peripheral vision (greyout) or by loss of central vision (blackout) to a white light with a luminance of 1.2×10^{-2} candles/cm (35.3 ft-L). The experimental design consisted of a 3-week ambulatory control period (C), 2 weeks of bedrest (BR1), followed by a 2-week ambulatory recovery period (R), then 2 weeks of bedrest with rehydration prior to centrifugation (BR2), and a final week of recovery. +Gz tolerance was measured immediately before and at the end of each bedrest period. The subjects ate a calorically controlled, nutritionally balanced diet and exercised ½ hr each day on a bicycle ergometer at 50 percent of their maximal oxygen uptake (approximately 450 kcal/day) during the entire study. The subjects were rehydrated with 1.0 to 1.9 liters of a drink, containing 143 meq ℓ Na, 31 meq ℓ K, and a total osmolarity of 620 mOsm/ℓ, given over a 3-hr period before centrifugation in BR2.

There were significant ($p < 0.05$) reductions in average +Gz tolerances following both bedrest periods at all three G levels. Compared with control values, following BR1, average ramp plus plateau tolerances decreased 36 percent at 2.1 G, 30 percent at 3.2 G, and 44 percent at 3.8 G. Compared with recovery values, following BR2, average tolerances decreased 23 percent at 2.1 G, 29 percent at 3.2 G, and 34 percent at 3.8 G. Rehydration increased tolerance ($p < 0.001$) only at 2.1 G, but tolerance was not completely restored to control values. Compared with control values, average tolerances at all three G levels were lower after the recovery period, suggesting that 2 weeks of recovery is not long enough to permit tolerance to return to pre-bedrest levels. After bedrest the time full visual capability can be maintained at plateau during these acceleration profiles can be estimated from the equation: tolerance (sec) = 345 + (1605/G level). In relaxed deconditioned men without protective garments, tolerance at 2.0 G is 7.6 min and the level of instant blackout is about 4.7 G. It is concluded that 2 weeks of bedrest results in a significant decrease in centrifugation to tolerance which occurred despite the use of moderate daily isotonic exercise. Compared to nonhydration control values, rehydration significantly improves +Gz tolerance only at 2.1 G but did not return tolerance to ambulatory control levels.

76. Greenleaf, J. E., H. L. Young, E. M. Bernauer, R. H. Armbruster, L. A. Sagan, R. W. Staley, L. Juhos, W. van Beaumont, and H. Sandler. Effects of isometric and isotonic exercise on body water compartments during 14 days bedrest. Aerospace Medical Association Preprints, 1973, pp. 23-24.

Summary: Plasma volume (Evans blue space) and extracellular fluid volume (bromide space) were measured periodically in seven men who underwent a 14-day ambulatory control period, three 14-day bedrest periods separated by two 21-day recovery periods, and a final 4 days of recovery. During bedrest the subjects performed in the supine position (a) no exercise, (b) isometric exercise, and (c) isotonic exercise. Plasma and ECF volumes decreased on day 4 of bedrest. At the end of bedrest, plasma volume remained depressed while ECF and interstitial fluid volume returned to pre-bedrest levels. The two exercise regimens retarded the drop in plasma, ECF, and ISF volumes. Factors other than osmotic pressure must be involved in the fluid shifts observed during bedrest, because, by the third day of bedrest, hematocrit and plasma osmolarity were elevated and the initial diuresis has subsided. Since ECF volume was restored to control levels by the end of bedrest in the presence of hypovolemia, it appears the controlling mechanism for fluid distribution is influenced by the total ECF rather than the plasma volume.

77. Griffith, D. P. Immobilization hypercalciuria: Treatment and a possible pathophysiologic mechanism. *Aerospace Medicine* **42:1322-1324, 1971.**

Purpose: To test the hypothesis that contraction of the extracellular fluid volume should reduce the hypercalciuria during recumbency.

Procedure and methods: Seven patients were used as subjects. Five were paralyzed from recent spinal cord injuries and two were neurologically normal, but required prolonged recumbent immobilization for orthopedic reasons. The patients ate a diet containing 600 to 800 mg Ca/day and were hypercalciuric (greater than 300 mg/day). During the control periods the subjects had ad libitum NaCl intake. During the treatment period, the patients were given 1.0 g NaCl/day in the diet and/or hydrocholorothiazide, 50 mg twice daily. All patients had indwelling urethral catheters.

Results: Urinary Na and Ca were reduced and 58 and 53 percent, respectively, in the five paralyzed patients by combined use of a low sodium diet and the thiazide diuretic. In two paralyzed patients, Ca excretion was reduced solely by the low salt diet, but a further reduction was achieved by addition of the thiazide diuretic. In one paralyzed patient, Ca excretion promptly increased to control levels with cessation of the low salt intake.

Conclusions: In recumbent patients, calcium excretion is reduced independently by a low salt diet and by a thiazide diuretic, but neither treatment alone is as effective as the combination of the two. Possible pathophysiologic mechanisms are chronic recumbency and/or weightlessness, intercompartmental fluid and electrolyte shifts, relative ECV expansion, diminished Ca reabsorption in proximal nephron, and hypercalciuria with secondary hyperparathyriodism, increased osteolysis, or bone demineralization.

78. Gunther, O. and R. Frenzel. Über den Einfluss langer andauernder körperlicher Inaktivitat auf die Kohlenhydrattoleranz. *Zeitschrift für die gesamte innere Medizin* 24:814-817, 1969.

Authors' abstract: The influence of prolonged bodily inactivity on carbohydrate tolerance was investigated. Prednisone-glocuse-tolerance tests were conducted at 4-week intervals on 20 patients confined to bed for at least 8 weeks because of diseases known not to have any direct influence on carbohydrate metabolism. In two cases, the patients were re-examined 2 yr after remobilization. The following results were obtained: (1) Reductions in carbohydrate tolerance can be brought about by prolonged bodily inactivity alone. (2) The more complete the immobilization and the longer it lasts, the greater is the impairment of carbohydrate metabolism. (3) Carbohydrate tolerance reductions due to confinement in bed are observed almost exclusively in older persons. (4) As a rule, these disturbances of carbohydrate metabolism are reversible after remobilization.

79. Gurfinkel, V. S., Ye. I. Pal'tsev, A. G. Fel'dman, and A. M. El'ner. Changes in certain human motor functions after prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:148-161, 1969.

Purpose: To investigate the influence of prolonged bedrest on the retention of such motor habits as maintaining the vertical position, walking, and rising from the supine position.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days) and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' summary: Prolonged hypokinesia results in disturbance of motor automatisms (synergies), as manifested in changes in such coordinated acts as standing up and walking and in the innervation relationships on which they are based. The physical-conditioning methods used in the experiments were quite effective in preventing gross motor disturbances.

80. Gurvich, G. I. and G. D. Yefinmenko. Brain hemodynamics during prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 1:62-66, 1967.

Authors' abstract: The rheoencephalographic technique was applied to a study of cerebral hemodynamics of four test subjects exposed to prolonged (up to 75 days) hypokinesia. Examinations were made prior to, during, and following the bedrest experiment. Observations also were made with the aid of orthostatic tests performed at the end of bedrest. The studies revealed a phasic pattern of changes of cerebral hemodynamics and their correlation with changes of higher nervous activity. In addition, the experiments revealed that the rheoencephalographic technique can be used for early diagnosis of intolerance to prolonged hypokinesia and precollaptoid states during orthostatic tests.

81. Haines, R. F. Effect of prolonged bedrest and $+G_Z$ acceleration upon peripheral visual response time. *Aerospace Medicine* 44(4):425-432, 1973 (also Haines, R. F. Effect of prolonged bedrest and $+G_Z$ acceleration on peripheral visual response time. NASA TN D-7161; Haines, R. F. Effect of bedrest and positive radial acceleration upon peripheral visual response time. Aerospace Medicine Association Preprints, 1972, pp. 116-117).

Author's abstract: Cardiovascular deconditioning, dehydration, and other physiological changes which occur as a result of prolonged exposure to the zero-G space environment raise some questions about the applicability of much previous research which has shown that spacecraft reentry accelerations pose no appreciable physiological or performance problems for the astronauts. The present paper deals with whether or not peripheral visual response time changes during $+G_Z$ acceleration after 14 days of bedrest. Eighteeen test lights, placed 10° arc apart along the horizontal meridian of the subject's field of view, were presented in a random sequence. The subject was instructed to press a button as soon as a light appeared. This testing occurred periodically during bedrest and continuously during centrifugation testing. The results indicated that (1) mean response time was significantly longer ($p < 0.01$) to stimuli imaged in the far periphery than to stimuli imaged closer to the line of sight during $+G_Z$ acceleration, (2) mean response time at each stimulus position tends to be longer at plateau G than during the preacceleration baseline period for that run by an amount which ranged from about 20 to 120 msec, (3) mean response time tends to lengthen as G level is increased, and (4) under these testing conditions peripheral visual response time during $+G_Z$ acceleration within approximately 40 sec of blackout does not provide a reliable indicator that blackout is going to occur. The bedrest response time data showed that the distribution of response times across the horizontal retinal meridian remained remarkably constant within subjects from day to day during the bedrest and recovery periods. These findings are discussed in relation to previous studies and to the design and placement of aerospace vehicle cockpit instruments.

82. Haines, R. F. Effect of bedrest and exercise on body balance. *Journal of Applied Physiology* 36:323-327, 1974.

Author's abstract: A battery of 11 body balance tests was administered to 7 men before and after 14 days of bedrest. Seven men who had not undergone bedrest served as controls. During bedrest, each subject underwent daily either isotonic, isometric, or no leg exercise. The results showed that, for the bedrested no exercise, isotonic exercise, and isometric exercise groups, 2 weeks of bedrest produces significant body balance decrements on 3, 4, and 5 of the 11 tests, respectively. Daily leg exercise did not prevent the debilitating effects of bedrest on body balance. After bedrest, balance skill was relearned rapidly so that, in most tests, performance had reached pre-bedrest levels by the third revovery day. The rail walk eyes open and the left leg rail balance eyes open tests were the most sensitive for measuring the effects of prolonged bedrest. These data suggest that balance impairment is not due to loss of muscular strength in the legs but perhaps to a bedrest-related change in the neurally coded information to postural control centers.

83. Halberg, F., C. Vallbona, L. F. Dietlein, J. A. Rummel, C. A. Berry, G. C. Pitts, and S. A. Nunneley. Human circadian circulatory rhythms during weightlessness in extraterrestrial flight or bedrest with and without exercise. *Space Life Sciences* 2:18-32, 1970.

Authors' summary: Human circadian rhythms are detected in heart rate and in the durations of electromechanical systole and of the entire cardiac cycle by an inferential statistical analysis, the cosinor method, carried out rapidly by computer. These findings apply to men on earth in bed for several days – whether or not they intermittently carry out isometric exercise. Rhythms also are demonstrated in men at a few hundred nautical miles from earth experiencing weightlessness for several days during extraterrestrial space flight; whether or not these circadian rhythms are 24-hr synchronized can not be discussed with the data on hand.

Such demonstrations of rhythm persistence in astronauts and cosmonauts underline the need for further work on mammals to define and to control these rhythmic factors affecting not only the longer-term scheduling of human activities in extraterrestrial space but also rhythmic behavior in health and disease on earth. The implementation of such studies by rigorous circadian and other parameter estimations carried out on earth remains a *sine qua non* at first; yet given such background information, the long-term behavior of rhythms in organisms transferred to terrestrial, lunar, and eventually solar orbits remains a major challenge to the United States program for research in extraterrestrial space as well as a fertile ground for future international cooperation, involving as it does phenomena directly related to human performance and resistance.

84. Heilskov, N. C. S. and F. Schønheyder. Creatinuria due to immobilization in bed. *Acta Medica Scandinavica* 151:51-56, 1955.

Purpose: To investigate nitrogen kinetics during bedrest.

Procedure and methods: Three healthy male medical students (20-23 yr) underwent a 14-day ambulatory control period followed by 16-18 days of bedrest. During bedrest, two subjects were encased in plaster of Paris casts on both legs. The controlled diet furnished about 500 mg creatine daily. Urinary and fecal nitrogen were determined on 24-hr samples. Urinary creatinine and creatine were also determined on 24-hr samples.

Results: Bedrest combined with immobilization of the lower extremities produced a negative nitrogen balance. The negative balance occurred after a latent period of about 5 days in all subjects and reached a maximum after about 10 days of immobilization.

The total nitrogen loss during bedrest in ES was 81 gm, in RB about 72 gm, and in FS about 27 gm.

There was essentially no creatine in the urine during the control period. During bedrest the daily excretion of creatine reached a maximum of 805 and 627 mg in RB and ES after they had been immobilized for 11 and 12 days, respectively, while FS reached maximum excretion of 714 mg on the 17th day.

Conclusions: It is not possible to reach a final decision whether the creatinuria is due to enhanced muscle destruction or to a reduced capability of utilizing the creatine supplied from the diet or formed in the organism.

85. Hoffler, G. W., R. A. Wolthuis, and R. L. Johnson. Effect of seven days of bedrest on cardiovascular responses to lower body negative pressure. Aerospace Medical Association Preprints, 1971, pp. 174-175.

Purpose: To quantitate alterations in human orthostatic tolerance, determined by lower-body negative pressure (LBNP) stress, following 1- and 7-day bedrest periods.

Procedure and methods: Nine healthy U.S. Air Force subjects underwent LBNP tests immediately after four centrifugation tests conducted to tolerance. Two of these tests preceded the periods of enforced bedrest and provided normal, baseline control data. The other two tests were conducted approximately 21 days following completion of the bedrest study.

Measurements made during LBNP testing included (1) a Frank lead vectorcardiogram, (2) blood pressure by the Gemini system, indirect Korotkov sound technique, (3) precordial low-frequency heart sounds for estimating stroke volume, (4) bilateral calf circumference change by double-stranded mercury in rubber strain gauges, and (5) pressure change withing the LBNP device.

The test protocol lasted 25 min. The first 5 min were at ambient pressure, the next 15 at successive increments of LBNP (5 min each at −30, −40, and −50 mm Hg), and the last 5 min again at ambient pressure.

Results: Supine resting heart rate was significantly elevated (8 percent, $p < 0.05$) after 7 days of bedrest, while maximal heart rate during LBNP stress was even more significantly increased (26 percent, $p < 0.01$). Resting cardiac output was well maintained after bedrest; during LBNP cardiac output varied little more and no pattern emerged even for those cases of impending syncope. Eight of the nine subjects showed decreases (1.4 percent net) in their resting calf circumference after bedrest; no distinct alteration in venous compliance was evident. Resting pulse pressure was decreased (15 percent, $p < 0.05$) only after the long inactive period. Three subjects experienced presyncopal episodes during LBNP. All subjects completed the fifth LBNP test without incident and demonstrated a group response not significantly different from those obtained before bedrest.

Conclusions: The group response clearly indicates significant alterations following hypodynamia. Generally, these changes are more evident during the application of stress (LBNP). They are also clearly of greater magnitude after 7 days of bedrest than after only 1 day. Weight loss, particularly that of body fluids and especially of intravascular volume, is often considered a major causative factor in cardiovascular alterations under these conditions. LBNP as used in this study induced cardiovascular responses after prolonged hypodynamia quite like those seen during tilt-table stress. LBNP is especially well suited for providing varying levels of equivalent $+G_Z$ stress upon the cardiovascular system.

86. Howard, J. E., W. Parson, and R. S. Bigham, Jr. Studies on patients convalescent from fracture. III. The urinary excretion of calcium and phosphorus. *Bulletin of the Johns Hopkins Hospital* 77:291-313, 1945.

Authors' summary: The pattern of urinary excretion of calcium and phosphorus is described in patients immobilized in extensive casts after fracture of femur, tibia, and after femoral osteotomy. Urinary excretion of calcium rises steadily until the period of nitrogen wastage ends, after which it remains fairly constant for a prolonged period. This sustained excretion of calcium via the urine was but little influenced by dietary changes, administration of calciferol, or alkalis. The possible relationship between the blood supply to the immobilized part and the pattern of urinary calcium excretion is discussed.

87. Hulley, S. B., J. M. Vogel, C. L. Donaldson, J. H. Bayers, R. J. Friedman, and S. N. Rosen. The effect of supplemental oral phosphate on the bone mineral changes during prolonged bedrest. *Journal of Clinical Investigation* 50:2506-2518, 1971.

Purpose: To determine whether administration of oral potassium phosphate prevents the development of disuse osteoporosis during 210 days of bedrest.

Authors' abstract: Five healthy young men were studied during 24-30 weeks of continuous bedrest. During the first 12 weeks of bedrest, untreated subjects increased calcium excretion in the urine by 109 mg/day and in the feces by 147 mg/day. The rate of total body calcium loss was 0.5-0.7 percent per month. Losses of central calcaneus mineral, assessed by gamma-ray transmission scanning, occurred at a tenfold higher rate, whereas the mineral content of the radius did not change. Changes in phosphorus balance resembled the calcium pattern, and increased excretion of nitrogen and hydroxyproline also occurred during bedrest. Upon reambulation, the subjects' calcium balance became positive in 1 month and recovery of their calcaneus mineral was complete within 10-20 weeks.

Treatment with potassium phosphate supplements (1327 mg P/day) entirely prevented the hypercalciuria of bedrest, but fecal calcium tended to increase. During the first 12 weeks, calcium balance was slightly less negative (mean −193/day) than during bedrest without added phosphate (mean −267 mg/day). This effect was not seen during the second 12 weeks of bedrest. The patterns of magnesium excretion were similar to those of calcium. Fecal and urinary phosphorus excretions were doubled, and phosphorus balance became positive (+113 mg/day). Mineral loss from the central calcaneus was similar to that of untreated subjects. It is concluded that this form of phosphate supplementation reduces urinary calcium excretion but does not prevent bone loss during bedrest.

88. Hyatt, K. H., L. G. Kamenetsky, and W. M. Smith. Extravascular dehydration as an etiologic factor in post-recumbency orthostatism. *Aerospace Medicine* 40:644-650, 1969.

Purpose: To investigate the effect of 14 days bedrest on the production of orthostatic hypotension.

Procedure and methods: Twenty healthy men were tested during a 1-week ambulatory control period and 2-week bedrest period. The subjects ate a controlled diet during the entire study. Water and sodium balances were measured. Measurements made before and during tilting were plasma volume (I-131), EKG, heart rate, brachial and pulmonary arterial pressure, and cardiac output (indocyanine green). After recovery from tilting, the subjects exercised on a bicycle ergometer at 50 W and, after 4 min of exercise, cardiac output, heart rate, and the above pressures were measured. During the bedrest period, 10 of the 20 subjects received a daily dosage of 0.2 mg of 9-alpha-fluorohydrocortisone. The untreated subjects were the control group.

Results:

All subjects tolerated the non-instrumented tilt prior to entry into the study. However, there was a 50-percent incidence of syncope before as well as after bedrest when the subjects were tested with the cardiac catheter and arterial needle in place.

Treatment with 9-alpha did not change pre- or post-bedrest tilt tolerance.

After bedrest, during tilting, there was a significant ($p < .05$) decrement in the cardiac index ($L/(min \cdot M^2)$) and central blood volume and increase in heart rates and in peripheral and pulmonary vascular resistances.

In the subjects who tolerated 18 min of tilt, there was no difference in cardiac index or central blood volume compared with supine values.

After bedrest, during supine exercise, there were significantly smaller increments in the cardiac index and stroke volume (in fact, stroke volume did not differ from the resting value) and significantly greater elevation in heart rate.

During the first week of bedrest, the control group showed a significant decrease in plasma volume while the 9-alpha group did not. The decrease was not significant by the end of the 2-week bedrest period. Derived red cell volume was unchanged in both groups at any phase of the study.

Compared with ambulatory values, water balance became less positive by 200 to 300 ml during bedrest. The control and 9-alpha groups reacted similarly. Both groups exhibited highly significant decreases in sodium balance during bedrest of approximately 17 meq/24-hr, indicating an increased loss of sodium ions. Sodium and water losses were most profound during the first 2 days of bedrest and these balances never returned to control levels during the 2 weeks of bedrest.

Conclusions: The fluid loss must have been sustained by the extravascular compartments with resultant lowering of the tissue pressure. It is likely there was a large shift of plasma water into the lower extremity tissue spaces during post-bedrest tilting. The resultant decrease in plasma volume during tilt could account for the decrements in stroke volume and cardiac output during tilting and exercise.

89. Isabayeva, V. A. and T. A. Ponomareva. State of hemocoagulation and thrombocytes during hypokinesia after adaptation to high-mountain conditions. *Kosmicheskaya Biologiya i Meditsina* 7:53-58, 1973.

Authors' abstract: Short-term adaptation of test subjects to an elevation of 3200 m produced phasic changes in hemocoagulation and thrombocytes which included a relative decrease in blood-coagulating capacity and a progressive increase in the thrombocyte count. Further 10-day hypokinesia of test subjects preadapted to high altitude induced no disturbances in their coagulation system. Prolonged 24-day hypokinesia resulted in relative hypocoagulation (dropoff in plasma tolerance to heparin, increase in recalcification time) and decrease in the thrombocytogram. It was demonstrated that preliminary adaptation to high elevations can smooth marked shifts in hemocoagulation brought about by hypokinesia in untrained people.

90. Iseyev, L. R. and B. S. Katkovskiy. Unidirectional change in the human oxygen balance caused by bed confinement and restriction to an isolation chamber. *Kosmicheskaya Biologiya i Meditsina* 2:67-72, 1968.

Purpose: To investigate the effect of isotonic exercise on deconditioning during 20 days bedrest.

Procedure and methods: Four healthy men (21 to 32 yr) were restricted to the horizontal position for 20 days without exercise and for a second 20 days with daily isotonic exercise (300 kcal/day) using rubber exercisers. Exercise tolerance was measured with a modified step test involving 100 steps on a bench 25 cm high.

Results: Isotonic exercise of about 300 kcal/day performed by the subjects in the horizontal position retained submaximal exercise tolerance.

Authors' summary: Twenty-day bed confinement experiments revealed a relationship between changes in the human oxygen balance during physical work and the degree of restricted motor activity. A 120-day experiment conducted in an isolation chamber revealed similar changes in the oxygen balance, although the hydrostatic pressure of body fluids remained virtually unaltered and the test subjects were exposed to many other factors other than hypokinesia (isolation, modified atmosphere, etc.). The introduction of sanitary measures, including physical exercises, into the program of the 120-day experiment considerably improved the response of test subjects to physical loads. The similarity of oxygen balance changes in test subjects during hypokinesia and its improvement following physical exercises suggest that the changes are caused primarily by hypokinesia. It is indicated that the motor activity of spacecrew members during prolonged simulation experiments should be given special consideration in their work-rest schedules.

91. Iseyev, L. R. and Yu. G. Nefedov. Human tolerance to physical stress during four months isolation in a closed space. *Kosmicheskaya Biologiya i Meditsina* 2:42-46, 1968.

Authors' abstract: During the course of a 4-month experiment, the metabolic rate of test subjects exposed to isolation in an enclosure increased inadequately for the work performed. Also, energy expenditures involved in the work rose: light work required effort equivalent to a moderate load, while moderate loads became quite difficult. The physical performance and tolerance to muscular stress decreased significantly. This was manifested in the change of the standard indicators of the various functional systems, including gas and energy exchange. As experiment continued, the changes were aggravated. This should be taken into consideration when developing efficient work-rest cycles, food plans, and life-support systems for extravehicular space-suits and for spacecraft.

92. Issekutz, B., Jr., J. J. Blizzard, N. C. Birkhead, and K. Rodahl. Effect of prolonged bedrest on urinary calcium output. *Journal of Applied Physiology* 21:1013-1020, 1966.

Authors' abstract: The effect of prolonged supine position on the urinary nitrogen and calcium output was studied on young healthy men. Bedrest increased the excretion of calcium. The nitrogen output did not show any consistent response. Exercise on a bicycle ergometer in the sitting or supine position failed to change the course of calcium excretion. Supine exercise up to 4 hr/day did not decrease the urinary calcium output which was previously elevated by a complete bedrest. Quiet sitting for 8 hr combined with 16 hr lying did not prevent the rise of calcium output. On the other hand, 3-hr/day quiet standing proved to be sufficient to induce a slow decline of the elevated calcium excretion in four of five subjects. Following a complete bedrest in the recovery phase when the subjects resumed their normal up-and-about activities, both the nitrogen and calcium excretion rapidly decreased below the baseline value of the individual. It is concluded that the increase in urinary calcium output in prolonged horizontal position is due to the absence of longitudinal pressure (weight bearing) on the bones rather than the physical inactivity during bedrest.

93. Ivanov, I. I., B. F. Korovkin, and N. P. Mikhaleva. Investigation of certain biochemical blood serum indicators during prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:100-107, 1969.

Purpose: To investigate the activity of a number of enzymes and the contents of certain microelements in the blood serum during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results: Toward the end of the bedrest in groups II and III, a trend toward lower serum potassium content was noted. Increased activity of serum alkaline phosphatase was observed during bedrest. In this experiment, there were no changes in serum aspartate-amino-transferase, alanine-aminotransferase, aldolase, creatinekinase activity, sodium, phosphorus, calcium, urea, or the microelements (Cu, Mn, Al) in groups IV or V during bedrest.

94. Ivanov, L. A. Change in tissue oxygen metabolism during the initial period of hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 6:82-86, 1972.

Author's abstract: The effect of a 6-day bedrest experiment on external respiration and oxygen metabolism in the subcutaneous connective tissue was studied in healthy test subjects in the age group 24-35 yr. During a post-experiment oxygen inhalation test, the time interval in which arterial oxygen saturation attained a maximum tended to increase. This was indicative of certain limitations on external respiration functional capabilities: oxygen consumption decreased, spirographic oxygen deficiency increased, and the respiration level of the subcutaneous connective tissue slightly declined. After the 6-day bedrest experiment, oxygen supply and the oxygen tension level in the subcutaneous connective tissue remained virtually unchanged.

95. Jacobson, L. B., K. H. Hyatt, R. W. Sullivan, H. Sandler, S. A. Rositano, and R. Mancini. Evaluation of $+G_Z$ tolerance following simulated weightlessness (bedrest). NASA TM X-62,311, 1973, 75 p.

Authors' abstract: This study was undertaken to evaluate the magnitude of physiologic changes which are known to occur in human subjects exposed to varying levels of $+G_Z$ acceleration following bedrest simulation of weightlessness. Bedrest effects were documented by fluid and electrolyte balance studies, maximal exercise capability 70° passive tilt and lower body negative pressure tests, and the ability to endure randomly prescribed acceleration profiles of $+2G_z$, $+3G_z$, and $+4G_z$. Six healthy male volunteers were studied during 2 weeks of bedrest after adequate control observations, followed by 2 weeks of recovery, followed by a second 2-week period of bedrest at which time an Air Force cutaway anti-G suit was used to determine its effectiveness as a countermeasure for observed cardiovascular changes during acceleration. Results showed uniform and significant changes in all measured parameters as a consequence of bedrest, including a reduced ability to tolerate $+G_Z$ acceleration. The use of anti-G suits significantly improved subject tolerance to all G exposures and returned measured parameters such as heart rate and blood pressure toward or to pre-bedrest (control) values in four of the six cases.

96. Johansson, J. E. Daily fluctuations of metabolism and body temperatures in sober condition and complete muscular rest. *Scandinavisches Archiv für Physiologie* 8:85-142, 1898.

Author's abstract: The variation of the gaseous metabolism (release of CO_2), the secretion of N, and fluctuation of body temperature were investigated during periods of complete muscular inactivity and ordinary bedrest. It is shown that daily fluctuations of these values are primarily functions of the state of activity and largely independent of the time of the day, although they are affected to some extent by daylight, environmental noise, and mental activity. The regularity in metabolism and body temperature observed is interpreted as the adaptation of the organism to varying conditions and not as the expression of some unknown factor controlling daily periodicity.

97. Johnson, P. C., T. B. Driscoll, and W. R. Carpentier. Vascular and extravascular fluid changes during six days of bedrest. *Aerospace Medicine* 42:875-878, 1971.

Authors' abstract: Body fluid spaces were determined before and after 1 and 6 days of bedrest. All fluid spaces were calculated and compared on the basis of fluid volume per kilogram body weight. The nine male subjects who particpated in the study were divided into two groups according to their deviation from an ideal body weight as determined from individual heights. The subjects below ideal weight had a statistically greater mean ml/kg red cell mass, extracellular fluid volume, and total body water than the respective means from the group whose weights were above ideal. During bedrest a decrease of statistical significance was found in the plasma volume but not in the red cell mass, total body water, and extracellular fluid volumes. The data do not support the often stated theory of fluid and electrolyte diuresis as the cause of the slowly decreasing plasma volume loss found after the first 24 hr of bedrest.

98. Kakurin, L. I. Effect of long-term hypokinesia on the human body and the hypokinetic component of weightlessness. *Kosmicheskaya Biologiya i Meditsina* 2:59-63, 1968. (Same study as Cherepakhin 1968a, Cherepakhin 1968b, Petukhov *et al.*, 1963, and Georgiyevskiy *et al.*, 1968.)

Purpose: To determine the effectiveness of varied and very intensive muscular training as a remedial procedure for hypokinetic disorders in healthy human subjects undergoing 62 days of bedrest.

Procedure and methods: Six young, healthy men (22 to 36 yr) underwent 62 days of bedrest. Group A (three subjects) performed daily a group of isometric and isotonic physical exercises with rubber cords designed to stress all the major muscle groups. In addition, a bicycle ergometer was installed on each subject's bed and during the first 20 days the load was 700 to 800 kcal/day, then 900 to 1000 kcal/day for the next 20 days, and 1100 to 1200 kcal/day during the final 20 days. Group B (three subjects) was the non-exercise control group. The total daily energy expenditure was approximately 3400 kcal/day.

Results: In the exercise group, the work capacity increased during bedrest while the work capacity of the control group decreased markedly.

Centrifugation tolerance ($+G_X$) was reduced in the control group but unchanged from prebedrest levels in the exercise group.

In the exercise group, there was less of a decrease in the phagocytic activity of blood neutrophils and the bactericidal properties of the skin compared with similar measurements in the non-exercising subjects.

The exercise training was not able to prevent dehydration, the increased excretion of electrolytes, the reduced mineral saturation of the bones, the reduced muscle tone, and the increase in the pulse rate and systolic volume of the heart during rest.

Author's conclusions: To maintain the work capacity of a spaceship crew during a long flight or for increasing its tolerance to unfavorable environmental conditions, it is necessary to have a complex of active stimuli which include pharmaceuticals as well as physical exercises.

99. Kakurin, L. I., R. M. Akhrem-Akhremovich, Yu. V. Vanyushina, R. A. Varbaronov, V. S. Georgiyevskiy, B. S. Katkovskiy, A. R. Kotovskaya, N. M. Mukharlyamov, N. Ye. Panferova, Yu. T. Pushkar', Yu. A. Senkevich, S. F. Simpura, M. A. Cherapakhin, and P. G. Shamrov. The influence of restricted muscular activity on man's endurance of physical stress, accelerations and orthostatics. *Soviet Conference on Space Biology and Medicine*, 1966, pp. 110-117.

Purpose: To determine centrifugation tolerance, physical exercise capacity, and orthostatic tolerance following bedrest.

Procedure and methods: Four healthy men (22 to 24 yr) underwent 20 days of bedrest without physical exercies.

Results: The leg muscles showed the greatest loss of tone (7.8 to 11.6 percent and the arms the least decrease (1.0 to 3.7 percent).

Exercise total work decreased 26 percent after bedrest. The average maximal oxygen uptake was reduced from 3.1 to 2.7 liter/min (−12.9 percent).

Orthostatic tolerance was reduced after bedrest: greater tachycardia, a drop in pulse pressure, and less-prounounced skin temperature drop on the leg.

On the 14th day of bedrest, there was a higher elevation of both systolic and diastolic blood pressures during the cold pressor test, a threefold increase in peripheral resistance, and subjective complaints of tenderness not only in the immersed hand, but also in the entire arm up to the shoulder girdle.

100. Kakurin, L. I., B. S. Kamkovskiy, V. S. Georgiyevskiy, Yu. N. Purakhan, M. A. Cherenikhin, B. M. Mikhaylov, B. N. Pemukhov, and Ye. N. Buryikov. Functional disturbances during hypokinesia in man. *Voprosy Kurotologii Fizioterapii i Lechebonoy Fizicheskoy Kul'tury* 35:19-24, 1970.

Purpose: To differentiate the effects of change in hydrostatic pressure from those of decreased muscular activity during bedrest.

Procedure and methods: Six healthy male volunteers underwent 62 days of bedrest. Group I (three men) had no exercise while group II (three men) had a variety of physical exercises, including bicycle ergometry and isometric exercises. The intensity of the exercise increased from 800 to 1100 kcal/day at the end of the experiment.

Results:

Greater decrease in muscular tone compared to the exercisers.

Decrease in circumference of the skin of 3 cm compared with 2 cm with exercise.

Greater decline in strength than in the subjects who exercised.

Optical density of bone sample decreased by 10.5 to 20.7 percent compared to 2 to 7 percent decrease in the exercisers.

Oxygen uptake (basal metabolism) decreased in the control subjects and stabilized after 30 to 40 days.

Resting heart rate increased gradually over bedrest in the controls and, after a slight initial rise in the exercisers, stabilized during bedrest.

The exercisers had better orthostatic tolerance after bedrest than the controls.

The exercisers had better recovery following a standard bicycle ergometer test after bedrest. The working capacity of the exercisers after bedrest increased 4 percent while the controls decreased by 43 percent.

Disturbances induced by bedrest that were unaffected by physical training include changes in water-electrolyte balance and the functional state of the auditory analyzer.

101. Kakurin, L. I., B. S. Katkovskiy, A. N. Kozlov, and N. M. Mukharlyamov. Effect of hypokinesia on certain indexes of efficiency and respiratory function in man. *Aviation and Space Medicine,* 1964, pp. 192-194.

Purpose: To study physical work capacity during and after prolonged bedrest.

Procedure and methods: Four healthy men (21 to 24 yr) remained in bed for 20 days. Before and after bedrest the subjects were given an exercise step-test consisting of 100 climbs on a bench 25 cm high for 5 min (work rate, 400 to 500 kg-m/min).

Results: During bedrest there was a slight decrease in resting metabolism. After 20 days in bed, the standard step-test required much more effort than before the experiment as evidenced by increased oxygen uptake, marked increase in oxygen debt, and a decrease in the ratio of 0_2 uptake/0_2 debt. These changed responses were not fully restored to control levels during 10 days recovery.

102. Kalin, G. S. and V. G. Terent'yev. State of nervous-system functions during after effects of hypodynamia. *Problemy Kosmicheskoy Biologii* 13:215-220, 1969.

Purpose: To investigate neurological signs and symptoms resulting from prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' summary:

Distinct disturbances to the functions of the nervous system and the neuropsychic sphere were detected in subjects after prolonged (70-day) hypodynamia.

They were manifested chiefly in the appearance of organic microsymptomatics, asthenia, vegetative cardiac instability, and akinetic hypotrophy of the muscles of the lower leg.

After load tests administered at the end of hypodynamia (spinning on the centrifuge, passive orthostatic tests), the changes in the animal nervous system had increased.

There was a certain tendency to preferential weakening of the left (dominant) hemisphere of the brain (the appearance of occasional signs of dextral pyramidal and sinistral "cerebellar" insufficiency).

Subjects who participated in the hypodynamia experiments without preventive measures showed more pronounced functional disturbances; the disturbances were less pronounced when hypodynamia was combined with physical exercises on a treadmill and with autogenous conditioning.

After hypodynamia, the functions were restored in three phases, the basic content of which was as follows: vascular-vegetative dystonia and disturbed coordination of movements (first phase lasting from a few hours to 1-2 days), development of traumatic myositis in the lower extremities and vegetative-vascular instability (second phase, 3-4 weeks), and the appearance of symptoms of vegetative-vascular instability only during the load tests (third phase, 2-3 months).

Thus, the total duration of the aftereffect of 70-day hypodynamia ranged from 3-4 months for the various subjects.

103. Katkovskii, B. S. Effect of hypokinesia on human respiration in physical work. *The Oxygen Regime of the Organism and its Regulation,* edited by N. V. Lauer and A. Z. Kolchinskaya. Kiev: Naukova Dumka, 1966, pp. 231-235.

Purpose: To study the effect of prolonged bedrest on human respiration at rest and in physical work.

Procedure and methods: Two series of experiments involving four healthy men ages 21-32 were performed. The subjects were kept in bed in a horizontal position for 20 days. In the first series of experiments, their motor activity was restricted to a minimum. In the second series of experiments, the subjects performed a set of physical exercises using rubber shock absorbers while remaining in their horizontal position. The true caloric value of the set of exercises was 300 kcal/day on average. Respiration during physical work of medium intensity was studied by means of Belau's apparatus. During the subjects' stay in bed, spirometric studies were made of oxygen consumption under conditions of basal metabolism.

Results: First series: The subjects suffered considerably from the restriction of their motor activity. They showed pallor of the skin, loss of appetite, and constipation. Following the termination of bedrest, the dosed physical work became more difficult in all cases than before the experiment: there was an increased oxygen requirement during the work, an abrupt increase in oxygen debt, and decreased recovery coefficient and efficiency. The subjective difficulties during work were most pronounced on the first day following the termination of bedrest. The same period was marked by the greatest changes in the respiration during work.

Second series: The subjects tolerated their stay in bed much more easily than those in the first series. Their skin color was normal and their appetites good. During bedrest, they showed an increased oxygen consumption at rest. Objective examination did not show any deterioration in their respiration during physical work: the oxygen requirement of work remained practically unchanged, there was a slight decrease in the oxygen debt, and the recovery coefficient and efficiency remained about the same. Oxygen consumption at rest was somewhat higher after the experiment than initially.

Conclusion: A 20-day stay in bed with strict limitation of motor activity caused considerable changes in the respiration of the human body in physical work, including lower economy (increased oxygen requirement and decreased efficiency) and impaired quality of control, the satisfaction of the oxygen requirement of work now being more dependent on oxygen debt than prior to the experiment (increased oxygen debt and decreased recovery coefficient).

The set of physical exercises performed in a horizontal position during the stay in bed apparently balanced the effects of hypokinesia and preserved the subjects' stability to physical work at its initial level. The observed tendency to increased oxygen consumption at rest in a lying position, during the stay in bed, was probably due to an increase in the muscle mass of the body. The experimental data suggest that hypokinesia proper was the principal cause of the change in the respiration during physical work following a 20-day stay in bed. Apparently, the decrease in hydrostatic pressure of the blood column did not have any appreciable on the stability to physical work.

104. Katkovskiy, B. S. Human basal metabolism during prolonged bedrest. *Kosmicheskaya Biologiya i Meditsina* 1:67-71, 1967.

Purpose: To investigate the effect on basal metabolism of prolonged bedrest both with and without physical exercise.

Procedure and methods: Healthy men underwent 20 days (4 men, 22-25 yr) and 62 days (6 men, 22 to 37 yr) of bedrest. In the 20-day experiment, three subjects were subjected to $+G_X$ (chest to back) acceleration on a centrifuge with a radius of 7.5 m. The fourth subject was a control. The rate of acceleration was 6 G/min to 4G and 12G/min above 4G; the limit of tolerance was 14G. In the 62-day experiment, the men were divided into two groups: an exercise group and a non-exercise control group.

The exercise group performed 15-30 min of work in the morning and 1 to 2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased. The training was performed utilizing a bicycle ergometer, stretching springs and large rubber bands, and various static exercises. Bands with resistances of 7.5 to 15 kg were used to exercise the shoulder muscles and bands between 15 and 50 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercise. The average energy cost of the exercises was about 7.3 kcal/min (500 to 1000 kcal/day), with a total working time of 75 to 150 min/day.

The 62-day subjects underwent the same $+G_X$ acceleration profiles as the 20-day group. Caloric intake was 3000 to 3500 kcal/day. "Basal" metabolism was measured 20 to 25 min after awakening and evacuation of the bowel.

Author's summary:

The metabolic rate and pulmonary function of healthy test subjects were studied during 20- and 62-day-bedrest experiments, before and after which they were subjected to accelerations.

Three subjects who performed no physical exercises during the 62-day bedrest revealed a decreased metabolic rate and virtually unaltered pulmonary function.

Three test subjects who performed physical exercises during the experiments also manifested a reduction of oxygen consumption and metabolic rate beginning with the third 10-day period.

It appears very probable that the latter is unrelated to hypokinesia but is due to an increased physical conditioning or to adaptation to a changed hydrostatic pressure of body fluids.

105. Katkovskiy, B. S. and V. A. Andretsov. Pulmonary volumes of human subjects restricted to an antiorthostatic position with application of different counteracting agents. *Kosmicheskaya Biologiya i Meditsina* 6:55-59, 1972. (See Voskresenskiy *et al.*, 1972 for experimental design.)

Authors' abstract: Total lung capacity (TLC) and other pulmonary volumes of nine test subjects were studied during a 30-day-bedrest experiment. The subjects were fixed in their beds with the foot end being lifted at an angle of 4° to the horizontal. During the first experimental days, all parameters declined appreciable in the test subjects of all three groups. However, the pattern of changes in pulmonary volumes of the test subjects varied from group to group. The TLC of the first-group test subjects who performed physical exercise remained decreased until the end of the experiment; that of the second control group approximated the pretest level only on the 17th day, remaining still higher to the end of the experiment, and the TLC of the third-group test subjects who underwent electric muscle stimulation exceeded the pretest value of the fifth experimental day and continued to increase by the end of the experiment. Possible reasons for these changes are discussed. It is suggested that lung volume measurements can be used as an indirect criterion for determining central blood volume.

106. Katkovskiy, B. S., O. A. Pilyavskiy, and G. I. Smirnova. Effect of long-term hypokinesia on human tolerance to physical stress. *Kosmicheskaya Biologiya i Meditsina* 3:49-54, 1969.

Authors' abstract: A 62-day-bedrest experiment was performed on six healthy male test subjects. During the experiment an attempt was made to maintain high performance of three test subjects (first group) using physical exercises which compensated for their muscular inactivity (with respect to metabolic rates). The motor activity of the resting subjects (second group) was minimized. After the bedrest experience, the tolerance of the members of the second group to physical work decreased whereas the members of the first group retained tolerance to both moderate and heavy work. The experimental findings suggest that deterioration of the performance level of human subjects subjected to bedrest is due to hypokinesia.

107. Katkovskiy, B. S. and Yu. D. Pometov. Change in cardiac ejection under the influence of 15-day bed confinement. *Kosmicheskaya Biologiya i Meditsina* 5:69-74, 1971.

Purpose: To study changes in the principal parameters of human hemodynamics and gas exchange under the influence of a rigorous bedrest regime of moderate duration.

Procedure and methods: Five healthy males (24-30 yr) were subjected to 15 days of bedrest during which the food ration calorie content was 1800 cal/day. During recovery the motor activity regime was as usual and the daily calorie content was 2700 cal. Background data were determined for 10 days prior to the experimental period under clinical conditions.

Cardiac ejection was determined under the conditions used in ascertaining basal metabolism. Oxygen consumption and carbon-dioxide elimination, carbon-dioxide content in the final portion of exhaled air, and pulse rate were continuously registered for a period of 10-15 min. Thereafter, the subject in rhythm with a metronome performed return breathing into a rubber bag containing about 1 liter of a gas mixture: 3 percent CO_2, and 50 percent O_2 in nitrogen. The increse in CO_2 pressure in the bag-lung system was traced using an infrared low-inertia gas analyzer. Cardiac ejection and gas exchange were investigated on the third, sixth, and twelfth days of bedrest and the second day of recovery. The subjects were examined several months after the experiment ended under the same conditions.

Results: Beginning with the sixth day of bedrest, there is a reliable increase in the minute volume of circulation with a simultaneous decrease in oxygen consumption and a marked decrease in the O_2 and CO_2 arteriovenous difference. The changes in pulse rate were extremely insignificant. An analysis of the cardiac ejection indices reveals a substantial increase in cardiac stroke volume by the sixth day of bedrest, whereas the pulse rate remains virtually unchanged during the entire experimental period. During the recovery period there was a tendency to normalization of most of the registered indices, but the pulse rate was considerably higher than the initial level and was registered on the twelth day of bedrest; stroke volume was less.

Conclusions: During 15-day bedrest confinement, five men subjected to restricted motor activity exhibited a reliable decrease in oxygen consumption at rest. Beginning with the sixth day of bedrest, the cardiac ejection was higher than the initial level. Although the changes in the minute volume of circulation, stroke volume, and O_2 arteriovenous difference on the twelth day of bedrest were somewhat less clearly expressed than on the sixth, we cannot speak with assurance of any tendency to a normalization of the hemodynamic indices since this difference was statistically unreliable. It can only be assumed that the initial increase in stroke volume and minute volume of circulation is replaced by their decrease; then the process evidently assumes a wavelike character.

108. Katz, F. H. Adrenal function during bedrest. *Aerospace Medicine* 35:849-851, 1964.

Purpose: To measure plasma 17-hydroxycorticosteroids and cortisol and aldosterone secretory rates during 10 days bedrest.

Procedure and methods: Eleven men (17 to 23 yr) were studied before and on the tenth day of a 14-day-bedrest period. After 14 days of bedrest the subjects were divided into three groups: A, C and F. Groups C and F participated in an organized exercise program during the subsequent 4 weeks. Following this month of recovery, all groups returned to bed for two more weeks. During the second bedrest, group A did nothing, group C had cuffs inflated to 60 mm Hg pressure for 1 min out of every five from 0800 to 2200 hr daily, and group F performed standardized non-antigravity exercises and had the head of their bed tilted 10° from the horizontal to simulate lunar gravity. The subjects ate a constant diet with ad libitum salt intake and the ambient temperature during the bedrest periods was 75°–81°F. Measurements were made of plasma 17-hydroxycorticosteroids (17-OH-CS) and cortisol and aldosterone secretory rates.

Results: The circadian rhythm of plasma 17-OH-CS maintained its rhythm which was better established during the bedrest periods than during the period of ad libitum activity. There was no change in cortisol secretion rates during bedrest. Aldosterone secretory rate did not change with bedrest; however, there was a significant diminution of aldosterone secretion during the second bedrest period that was not related to the remedial treatments.

Conclusions: Inactivity from bedrest does not appear to change adrenal cortisol production. Inactivity from bedrest may change aldosterone production, but this is still equivocal.

109. Keys, A. Deconditioning and reconditioning in convalescence. *Surgical Clinics of North America* 25:442-454, 1945.

Author's summary:

Physical fitness is important for its own sake to the individual and to society. It may also be significant in resistance to disease and injury, but there is no close dependency of morbidity on fitness.

Deconditioning and reconditioning refer to loss and restitution of total physical fitness which comprises strength, endurance, speed, and coordination. The total bodily physiology contributes to these items but the muscular, cardiovascular, neuromuscular, and nervous systems are primary.

It is impossible to dissociate fitness from health by any fixed definition; fitness should be considered a component of total health. Disease and its treatment tend to produce deconditioning and this state may be prejudicial to recovery.

Bedrest of itself produces marked deconditioning involving metabolic, proprioceptor, and cardiovascular abnormalities as well as loss of fitness. Common practices of medical treatment tend to accentuate deconditioning but serious efforts should be made to correct this.

The appraisal of "condition" or physical fitness is difficult and the present state of knowledge is deficient. Clinical observations, the patient's subjective estimate, and special tests and measurements should all be employed.

The first attack on deconditioning should be to prevent or minimize its occurence. Under careful supervision it is usually advantageous to bring the patient quickly to a graduated program of activity. Exercise should be adjusted to produce some fatigue but not exhaustion.

A good and liberal diet is important and special attention should be given to appetite appeal for the convalescent. Vitamin supercharging and "super" diets are of unproven merit except in special cases of real nutritional deficiency.

It should definitely be a part of medical responsibility to restore the patient to full health and fitness as well as to remove or cure the primary disease or complaint.

Controlled experimental research on a large scale is badly needed in the whole field of fitness and of deconditioning and reconditioning.

110. Khilov, K. L., A. Ye, Kurashvili, and V. P, Rudenko. Influence of prolonged hypodynamia on the state of the vestibular analyzer. *Problemy Kosmicheskoy Biologii* 13:183-188, 1969.

Purpose: To study the influence of prolonged bedrest on vestibular-analyzer function.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs. The following tests were conducted: (a) Baramy rotation test, (b) threshold of galvanic current excitability, (c) otolith reaction, (d) Romberg test, (e) body balance and stability, and (f) caloric-nystagmus test.

Authors' conclusions: Prolonged hypodynamia influences the functional state of the vestibular analyzer. In some cases, the excitability of the vestibular analyzer increases during hypodynamia. Phases are observed in the excitability variations of the vestibular analyzer. The greatest functional changes are noted on the 7th, 10th, and 20th days of hypodynamia. The greatest degree of vestibular-function disorder was observed in persons who had shown asymmetry of the vestibular function prior to hypodynamia. The transition to active movement after hypodynamia again causes disturbance of the vestibular function; normalization takes at least 2-3 weeks.

Considering the nature of the sensory, animal, and vegetative reflexes, it may be concluded that the functions of both vestibular-analyzer receptors are disturbed during hypodynamia, but that the otolith apparatus is most strongly affected.

The caloric test, which was administered to the subjects repeatedly during hypodynamia, is not always harmless, and must therefore be used with great caution. Combined investigation, with attention to individual deviations, should be used in evaluation of vestibular-apparatus excitability during hypodynamia.

111. Klein, K. E., H. M. Wegmann, H. Brüner, and L. Vogt. Physical fitness and tolerances to environmental extremes. *Aerospace Medicine* 40:998-1001, 1969.

Authors' abstract: During "submaximum" loading tests of 20-30-min duration at simulated altitude (312 mm Hg) on the tilt table, during acceleration (2.5 $+G_Z$), and during exercise (17 kpm/sec) at sea level and at moderate simulated altitude (578 mm Hg), heart rates were significantly lower for highly trained athletes, 20-25 percent, than in nonathletes. In maximum tolerance tests, however, there was found only a significant difference between the two groups for maximum oxygen uptake at physical exercise, but no indication was seen for a positive cross adaption effect of physical exercise training on the other stressors. Statistical analysis of the correlation between heart-rate responses to the different stressors and the corresponding tolerances proved negligible relationships only, whereas heart rates were always highly dependent on sea level $\dot{V}O_{2max}$ ($r = -0.61$ to -0.83). The results do not support the idea of an improvement of human tolerance to environmental extremes by physical exercise training.

112. Korobova, A. A. and T. I. Goryunova. Change in precise movements in persons with different physical fitness when exposed to hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 3:41-45 1969.

Author's abstract: Changes in the coordination of athletes (runners and weight-lifters) exposed to a 40-day bedrest were investigated by the method of vector-operation dynamography. The tests were conducted before and after exercises (performed with a limited load with a bicycle-type erogometer and with a maximum load with a treadmill). A decrease in motor activity resulted in insignificant changes in the level of total error. Use of exercises of the two types helped to reveal qualitative differences (predominance of positive efforts) in the performance of the task.

113. Korobova, A. A. and Yu. B. Vinichenko. Dynamics of daily diuresis, creatinine excretion and mean thickness of the fatty skin layer in athletes subjected to prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 2:40-43, 1968.

Author's abstract: This study was made to determine the dynamics of daily diuresis, creatinine excretion, and mean thickness of the fatty skin layer in male athletes (runners and weight-lifters) during 40-day hypokinesia. Daily diuresis was determined with an accuracy to 1 ml, creatinine was assessed by the photoelectrocolorimetric technique, and the mean thickness of the fatty skin layer was measured with standard calipers. The difference between the mean values of creatinine excretion on different days of the experiment was not statistically significant. The diuresis level decreased in most test cases during the second part of the experiment. The mean thickness of the fatty skin layer increased. Insignificant fluctuations in creatinine excretion and increase in the mean thickness of the fatty skin layer indicate a reduction in protein synthesis, an increase in decomposition processes, and replacement of a part of the muscle tissue by fat. The decrease in daily diuresis by the end of the experiment occurs due to a changed level of fat metabolism and the Gauer-Henry reflex.

114. Korobkov, A. V., L. A. Ioffe, M. A. Abrikosova, and Yu. M. Stoyda. Dynamics of orthostatic tolerance of athletes after forty-day hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 2:33-40, 1968.

Purpose: To investigate the effect of 40 days of bedrest on changes in cardiovascular function during orthostatic tests.

Procedure and methods: Ten highly trained athletes, five medium- and long-distance runners (25 to 40 yr) and five weightlifters (24 to 36 yr) were subjected to 40 days of bedrest. The subjects were allowed to get out of bed once a day for 5 to 7 min for emunctory functions. The passive orthostatic test was given (a) in the horizontal position; (b) a 20° head downward position for 5 min, and (c) a 70° head-up position both before and after bedrest.

Results: After bedrest the ECG results indicate moderate hypoxia of the myocardium of the left ventricle. The velocity of the pulse wave in peripheral vessels increased, particularly in the ascending aorta. There was also an increase in systolic and diastolic pressure more clearly expressed among the weightlifters. During orthostasis after bedrest the subjects ECG showed some T-wave depression and increased myocardial hypoxia compared with the horizontal position. Heart rate was increased. The increase in heart rate after bedrest during orthostasis in weightlifters was significantly lower than among the runners.

Conclusions: It can be postulated that the character of the ECG changes after bedrest is affected by a relative intensification of sympathetic effects and a more marked decrease in the volume of filling of the ventricles associated with a deterioration of the functional state of the venous system. The greater stability of the venous system among the weightlifters may be associated with the increased efficiency of the muscle pump because of their well-developed muscles. The repeated Valsalva maneuvers utilized during weightlifting probably exert a conditioning effect on the venous circulation.

115. Korolev, B. A. Changes in cardiac activity during prolonged hypokinesia (Data from vector analysis). *Kosmicheskaya Biologiya i Meditsina* 2:52-55, 1968.

Author's abstract: It is known that long-persisting hypokinesia causes certain changes in the electrocardiogram: a decreased amplitude of the R and T waves, an inversion of the ST segment and T wave, and an increased U wave. For the purpose of determining the nature of the changes, the integral QRS and T vectors and the ventricular gradient in the frontal plane were studied for healthy male test subjects restricted to 70-day bed confinement. The values of the QRS and T vectors and the ventricular gradient decreased, the QRS vector being more often shifted to the right and the T and G vectors to the left. The angular distance between QRS, T, and G varied over a wide range. Distinct decrease of the vector values and increase in angular distances were observed during the third-fifth and seventh-ninth weeks. The changes in vectors, ventricular gradient, and angular distances were less in test subjects who regularly performed physical exercises during the bedrest experiment. The vector analysis revealed that the secondary nature of the changes in the electrocardiogram appear to be related to variations in myocardial metabolism. The reason for these changes is not organic impairment in the cardiac muscle, but function shifts, in all probability in water and salt metabolism. Changes in the concentration of potassium and sodium can result in impairment of the K^+ and Na^+ cellular gradient and the transmembrane potential; the latter causes changes in the ECG elements. This mechanism apparently is responsible for the decrease in the amplitude of the R and T waves and ST segment and other EKG changes during long-term hypokinesia.

116. Korolev, B. A. Changes in myocardial repolarization in healthy persons during restriction of motor activity. *Kosmicheskaya Biologiya i Meditsina* 2:81-85, 1968.

Purpose: To investigate the repolarization process of the heart in subjects during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs. The electrocardiogram was taken each week with 15 leads under basal conditions. The EKG was also taken after the subjects breathed a mixture of 90 percent nitrogen and 10 percent oxygen for 10 min.

Results: The results indicate a change in the repolarization process during bedrest. Most subjects exhibited an increase in the amplitude of the U wave, a lengthening of the aT-aU and S-aU intervals, and a decrease in the RR/S-aU ratio. A positive Tv, < Tv_6 syndrome was observed rather frequently in the subjects. The most clearly expressed deviations from normal were in the changes in the duration of the S-aU segment (they attained 0.04 to 0.06 sec).

Conclusions: It was concluded from circumstantial evidence that the change in the process of myocardial repolarization was the shifts in the electrolyte balance.

117. Korolev, B. A. Pattern of changes of electrocardiograms and cardiac contraction phases during orthostatic tests after longerm hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 3:67-71, 1969.

Purpose: To investigate changes in heart function during 70 days bedrest from the electrocardiogram.

Procedure and methods: Sixteen men (20 to 25 yr) were subjected to 70 days of strict bedrest with periodic 15-min, 75°, head-up tilting with the subjects sitting on a seat. During tilting, the electrocardiogram was taken and a vector analysis of the EKG was made in the frontal plane.

Results:

Orthostatic intolerance increased with the increase in the duration of bedrest.

During tilting, the EKG changes showed a well-defined tachycardia, slowing of atrioventricular conductivity, and conductivity along the right part of the bundle of His and a lengthening of electric systole by 0.04 to 0.06 sec. High acute $P_{2,3}$ aVF waves were registered during tilting; $Q_{2,3}$ waves appeared, the amplitude of the $R_{2,3}$ aVF waves increased, the height of R_1 decreased and the S_1 wave deepened. The S-T segment was displaced below the isoelectric line in leads 2,3 aVF, $V_{5,6}$ and displaced above the isoelectric line in leads aVL and aVR. The $T_{2,3}$, aV, T, and V_6 waves became negative, the TV_{1-3} waves were high, acute and equilateral but the TV-TV_6 syndrome was positive. The axis of the QRS complex was displaced to the right and rotated clockwise about the longitudinal axis.

Vector analysis revealed a marked rotation of the QRS vector to the right and the T vector to the left; the value of the vectors decreased and there was an increase in the angular distance between the QRS and T wave and between the QRS and the ventricular gradient. The ratio of the gradient to the QRS vector decreased 40 to 80 percent. With the increased duration of bedrest, the angular distances between the vectors became greater.

(same as A. R. Kotovskaya et al. Changes in the tolerance of man to transverse acceleration following hypodynamia of varying duration. 18th International Astronautical Congress, Belgrade, Yugoslavia, Sept. 1967, p. 131).

Authors' abstract: This work presents study of the capacity of 20 men to withstand transverse stresses ($+G_X$) after hypodynamia placed in a supine position for a length of 3 to 60 days. Gradual reduction in the resistance to the action of maximum stresses was detected at time periods of hypodynamia from 7 to 15-20 days. Later resistance to stresses was preserved approximately at the same level up to the 60th day of hypodynamia. Similar shifts were obtained in a study of the reactivity of the cardiovascular and breathing systems to stresses determined according to the level of pulse strain and increase of pulmonary ventilation before and after hypodynamia of varying duration. The results obtained give a basis for supposing the existence in the process of hypodynamia of two phases in reactions of an organism to stress. In the opinion of the authors, the presence of the second phase (stabilization) may support the development of a unique adaptation to conditions of hypodynamia.

122. Krasnykh, I. G. Influence of prolonged hypodynamia on heart size and the functional state of the myocardium. *Problemy Kosmicheskoy Biologii* 13:65-71, 1969.

Purpose To investigate heart size during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9-16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two gorups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results:

Prolonged bedrest leads to substantial hemodynamic abnormalities, with the result that heart size decreases by 13-20 percent.

The contractile function of the myocardium changed in all subjects. Physical exercises combined with medication resulted in less significant reduction in both heart size and contractile function.

The decrease in heart area when a set of prophylactic measures was taken (physical exercises + femoral cuffs + complex medication) was essentially the same as in the control group.

Restoration of heart changes to normal took 1 month in the subjects in group II (medication) and group III (treadmill exercise). In the subjects in the control group and groups IV and V, normalization was complete after 2 months of recovery.

Conclusion: Prolonged bedrest results in profound and serious disturbances of myocardial function that physical exercise helps ameliorate.

123. Krasnykh, I. G. Mineral saturation of bone tissue under conditions of prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:94-99, 1969.

Purpose: To investigate the problem of decalcification during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Author's summary: The mineral-saturation level of the right calcaneus and the first phalanx of the fifth finger of the right hand was studied by x-ray photometry in individuals subjected to prolonged hypodynamia. It was established that 70-73 days of hypodynamia reduced the amount of calcium salts in the calcaneus by an average of 11.8 percent and in the first phalanx of the fifth finger by 6.9 percent. Recovery of the calcium salts to the initial level was not complete a month later.

Use of complex preventive medication did not favorably influence the level of decalcification by comparison with a control. Physical exercises prescribed for prophylactic purposes and a combination of exercise with inflatable femoral cuffs and medications resulted in smaller (by factors of 2 to 5) losses of phosphorus and calcium salts by comparison with the control.

124. Krasnykh, I. G. Cardiac deconditioning during prolonged hypodynamia. *Voyenno-Meditsinskiy Zhurnal* 12:54-56, 1973.

Abstract: The influence of 30-day hypodynamia on heart size, stroke volume, and myocardial contractility was the objective of these experiments. The subjects were 20 healthy male volunteers divided into three groups. Members of the first group stayed in bed during the whole experiment, the men of the second group were free to move in a small chamber, and members of the third group stayed in bed and performed daily intensified physical exercises. Teleroentgenokymograms were used to determine the heart size (systolic and diastolic) and the stroke volume. The data obtained (tabulated) indicate that by the end of experiment the heart size of the men in the first group was reduced by about 20 percent and stayed at this level during the next month. The men also complained of dyspnea and tachycardia during physical loading, particularly during the first 10 days after the experiment. A similar reduction (about 10 percent was experienced by the test subjects of the second group, while in the third group these changes were insignificant. Complete restoration of heart size and stroke volume required 60 days. Daily exercises (the third group) almost fully prevented the development of cardiac deconditioning.

125. Krasnykh, I. G. Roentgenological study of cardiac function and mineral saturation of bone tissue after 30-day hypokinesia. *Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina* 8:68-71, 1974.

Author's abstract: Before and on the fourth day of a 30-day-bedrest experiment, the cardiac size and output, as well as the contractile function of the myocardium, were measured using teleroentgenokymograms. Bone density of the right heel bone and the first phalanx of the fifth finger on the right hand was determined roentgenophotometrically. In the early recovery period, the cardiac size, cardiac output, and the force of cardiac contractions decreased whereas the heart rate increased. Bone density also decreased. The countermeasures applied–physical exercises, lower body negative pressure, and muscle electro stimulation–reduced the mentioned changes but did not eliminate them entirely.

126. Krupina, T. N., B. M. Fedorov, T. V. Benevolenskaya, O. I. Baykova, V. S. Nevstruyeva, Ye. N. Kul'kov, R. S. Morozov, and V. S. Romanvov. Changes in cardiac activity during prolonged restruction of motor activity. *Kosmicheskaya Biologiya i Meditsina* 5:76-81, 1971.

Purpose: To investigate changes in cardiac activity during 120 days of bedrest on man and on rabbits.

Procedure and methods: Human experiments – Ten healthy men (22 to 44 yr) adhered to a rigorous 120-day bedrest regime. During bedrest, 6 of the 10 subjects received hormonal drugs (unspecified). Animal experiments – Sixty rabbits were confined in special cages that sharply restricted their mobility.

Results: Human experiment – The control ECG for all subjects was normal. At the end of bedrest, heart rate for half the subjects was the same as control but in the other half it was elevated 10 to 20 beats/min. Atrioventricular and intraventricular conductivity time remained at the control levels. Cardiac electric systole remained within normal limits. During bedrest in 9 of the 10 subjects, the amplitude of the T waves was decreased in the first standard and left unipolar chest leads. In 8 of the subjects, restoration of the control level for the T waves did not occur until 60 days of recovery. During bedrest, a significant decrease in the R waves was detected in only three subjects. By the third week of bedrest, all subjects exhibited objective indications of autonomic nervous system impairment: non-uniform skin coloring, skin blueness on the feet and hands, and increases sweating on the distal parts of the extremities. Later during bedrest these manifestations of autonomic – vascular dysfunction increased. By the end of 60 days, there was an increase in the tendon reflexes and, in two subjects, an asymmetry of the tendon reflexes was noted and Babinski's reflex was present. There was a decrease in muscle tone of the extremities and by the end of 120 days the circumference of the lower extremities had decreased an average of 5 to 6 cm.

Animal experiments – (1) during hypokinesia there were profound changes in catecholamine metabolism. By the 14th day of hypokinesia, myocardial noradrenaline was reduced by half while the myocardial adrenaline content was unchanged. By the 30th day of hypokinesia, the adrenaline content of the suprarenals had decreased slightly more than half. (2) With stimulation of different hypothalamic centers the thresholds of hypothalamic electric stimulation are increased. (3) By the 12th day of hypokinesia, the peripheral plasma concentration of 11-oxycorticosteroids was also reduced by half and by more than threefold by the 30th day. (4) Electron microscopic examination of the myocardial ultrastructures of rabbits sacrificed on the 14th day of hypokinesia revealed focal changes in the trophic apparatus of the muscle fibers (the mitrochondria), in the myofibrils, and in the capillaries.

Conclusions: The T-wave flattening in the men was probably not due to impairment of potassium metabolism or to hypocalcemia. It was probably the result of impairment of the sympathetic nerve function on the heart, expecially on mitochondrial function. Both decreased sympathetic function and a decreased energy supply can cause flattening of the T waves.

127. Krupina, T. N. and A. Ya. Tizul. Changes in the nervous system during a 120-day clinostatic hypokinesia and the prophylaxis of hypokinesic disorders. *Zhurnal Nevropatologii i Psikhiatrii* 71:1611-1617, 1971.

Authors' abstract: The authors studied the basic changes of the nervous system during a 120-day clinostatic hypokinesia and the effect of certain pharmacological preparations (pituitrin, deoxicortical steroid acetate, and nerabol) in the dynamics of hypokinesic disorders. The neurologically healthy men, ages 21 to 44, were test subjects; they were divided into three groups, one being a control group receiving no medication. As the experiment progressed there was an increase in the vegetative-vascular, electrolytic-humoral disorders and asthenization of the organism as well as a reduction in muscular tone, especially of the knee and femur. A gradual increase in neurological disturbances was observed toward the end of the third month and the beginning of the fourth. Most of the hypokinesic disturbances disappeared by the end of the second month following completion of the period of hypokinesia. The authors conclude that certain pharmacological agents with a wide action spectrum can be used to prevent hypokinesic disorders.

128. Krupina, T. N., A. Ya. Tizul, N. M. Boglevskaya, B. P. Baranova, E. I. Matsnev, and Ye. A. Chertovskikh. Functional changes in the nervous system and functioning and certain analyzers in response to the combined effect of hypokinesia and radial acceleration. *Kosmicheskaya Biologiya i Meditsina* 1:61-66, 1967.

Purpose: To investigate the functional state of the cerebral cortex and acceleration tolerance after prolonged bedrest.

Procedure and methods: Six healthy men (22 to 36 yr) were used as subjects and most had engaged in sports. They remained in bed for 62 days and three men were nonexercise controls. The exercise group performed 15-30 min of work in the morning and 1 to 2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased.

The training was performed utilizing springs and large rubber bands. Bands with resistances of 7.5 to 15 kg were used to exercise the shoulder muscles and bands between 15 and 50 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercise. The average energy cost of the exercises was about 7.4 kcal/min, (500 to 1000 kcal/day) with a total working time of 75 to 150 min/day. The calorie intake was 3000 to 3500 kcal/day.

Measurements made were electroencephalography, audiometry, muscular tone, responses to Coriolis accelerations, muscle girth, body balance, and tolerance to $+G_X$ accleration. The rate of acceleration was 0.15 to 0.20 G/sec.

Results: During bedrest in combination with relative isolation resulted in autonomic-vascular disorders and manifestations of asthenization, which appeared earlier and disappeared in subjects who did not perform physical exercises.

Auditory thresholds were raised from 15 to 34 decibels in all subjects, in most cases at the higher frequencies (2000 to 8000 cps). The maximal increase of the auditory thresholds appeared on the 5th and 41st days of bedrest. In four subjects hearing returned to normal by the end of bedrest and the remaining two after 2 weeks of recovery.

There was a decrease in tolerance to Coriolis and linear accelerations, most clearly expressed in those subjects who had not performed physical exercises. Tolerance to linear acceleration was restored by the second week of recovery. Tolerance to Coriolis acceleration in four subjects was restored to normal after 6 to 8 weeks. In the remaining two subjects, Coriolis tolerance had not returned to normal at 16 weeks of recovery.

129. Kus'min, M. P. Reactions of eye retinal vessels and intraocular pressure during man's 120-day restriction to a horizontal position. *Kosmicheskaya Biologiya i Meditsina* 7:65-69, 1973.

Author's abstract: This paper gives the results of measurements of diastolic pressure in the central retinal artery, blood pressure in the brachial artery, caliber of retinal vessels and intraocular pressure in 10 healthy male test subjects during a 120-day-bedrest experiment. Simultaneous phasic changes in the above indices gives evidence of a shift in the tone of retinal vessels. At the end of the bedrest experiment and during recovery, these indices were similar to the reference levels. During the experiment the intraocular pressure increased, attaining the upper normal limit. In two persons this increase was accompanied by visual disturbances.

130. Lamb, L. E. An assessment of the circulatory problem of weightlessness in prolonged space flight. *Aerospace Medicine* 35:413-419, 1964.

Author's summary: The problem of the circulatory aspects of weightlessness has been discussed. It has been emphasized that most observations to date have been directed toward orthostatic intolerance. For this reason, a review of the more important basic mechanisms associated with simple syncope or orthostatic intolerance has been included.

It has been emphasized that it has not at this date been proved that weightlessness associated with space flight is responsible for orthostatic intolerance. The report includes a critical analysis of the multiple factors associated with manned space flight. It is emphasized that the flights to date have also been associated with significant immobilization and inactivity of the space crewman. It is also emphasized that other environmental factors have been changed, including the gaseous environment and baraometric pressure. It has been pointed out that orthostatic intolerance or syncope is a symptom that can originate from multiple factors. The observation of transitory orthostatic symptoms in itself frequently does not permit a definitive answer relative to etiology.

This report has pointed out that the majority of experimental work done to date has involved changes in multiple environmental factors. Because bedrest experiment, water immersion experiment, and all other experiments of this type have essentially involved immobilization and inactivity as well as relative absence of vertical G stimulation, the relative influences of these multiple environmental changes on the incidence of subsequent syncope cannot be determined.

It has been emphasized that multiple instrumentation procedures used during experimental studies complicates the experimental design and nullifies interpretation. These procedures are useful in studying syncope, but artificially destroy the experimental design in the study of orthostatic tolerance.

It has been emphasized that orthostatic tolerance tests in tilt-table procedures are in no way analogous to transverse G tolerance required for reentry for most planned manned space missions.

Having laid this background of clarification of some of the facets of the problem of space flight relative to the circulatory system, subsequent articles in this series will report experiments relative to the assessment of the problems encompassed in prolonged manned space flight.

131. Lamb, L. E. Hypoxia -- an anti-deconditioning factor for manned space flight. *Aerospace Medicine* 36:97-100, 1965.

Purpose: To review the differences between the deconditioning syndrome and the syndrome of acclimatization by prolonged hypoxia, thereby suggesting a means of counteracting at least a portion of the problem of deconditioning.

Author's summary: Physiological deconditioning results in a clinical picture of decreased biological activity, manifested by decreased plasma volume, decreased red blood cell mass, decreased red blood cell production with inactive bone marrows, increased resting heart rate, decreased exercise tolerance, decreased orthostatic tolerance, decreased coronary blood flow, increased storage of catecholamine products in the myocardium, decreased muscle mass and muscle tone with resultant increased nitrogen excretion, and increased calcium mobilization with increased calcium excretion. Acclimatization produces clinical features which are exactly opposite of those noted in deconditioning. Acclimatization results in increased organ activity with increased bone marrow activity and erthopoiesis with increased red blood cell mass and increased blood volume. With acclimatization there is a tendency toward vagotonia with decreased heart rate. There is an increased exercise tolerance and an increased coronary blood flow. These observations suggest that prolonged hypoxia of a sufficient degree to produce suitable acclimatization is a useful agent in preventing deconditioning during manned space flight and in those situations on earth that result in deconditioning.

132. Lamb, L. E., R. L. Johnson, and P. M. Stevens. Cardiovascular deconditioning during chair rest. *Aerospace Medicine* 35:646-649, 1964.

Author's abstract: Six healthy subjects were studied in a simple, uncomplicated experiment using strict chair rest with immobilization as a means of achieveing physical inactivity. The normal bedrest period for sleep was permitted for each 24-hr period. All six subjects had normal orthostatic tolerance by routine tilt-table studies prior to the inactivity.

Five of the six subjects showed manifestations of orthostatic intolerance after approximately 4 days of the experiment. These manifestations ranged from dizziness to fainting and circulatory collapse. Nausea and vomiting were also seen.

This study demonstrates that simple physical inactivity of sufficient degree over a short period of time, uncomplicated by the problems of weightlessness or simulated weightlessness, will cause adverse changes in circulatory dynamics leading to syncopal reactions or circulatory collapse.

132. Lamb, L. E., R. L. Johnson, P. M. Stevens, and B. E. Welch. Cardiovascular deconditioning from space cabin simulator confinement. *Aerospace Medicine* 35:420-428, 1964.

Author's summary:

A group of 36 subjects undergoing space cabin simulator studies were examined in detail pre- and post-confinement. This group demonstrated cardiovascular deconditioning similar to studies noted in bedrest and other immobilization experiences.

Cardiovascular deconditioning effects occur in the presence of normal G-force application in subjects undergoing a normal 24-hr day cycle with frequent periods of sitting upright and intermittent work-sleep periods. This demonstrated that the prone body position or weightlessness was not necessary to produce these manifestations of deconditioning.

Cardiovascular deconditioning as noted in this study complicated by given chamber environments included the following: decreased blood volume, decreased hemoglobin, decreased hematocrit, decreased exercise tolerance manifested by increased pulse rate after Master's exercise tolerance test, decreased exercise endurance on the treadmill, decreased maximum oxygen consumption, and decreased orthostatic tolerance.

Decreased orthostatic tolerance was manifested by an increased incidence of syncope. Twenty-five percent of the subjects had syncopal episodes on a simple tilt-table test after deconditioning. The remainder of the subjects as a group manifested during orthostasis increased heart rate, decreased pulse pressure, and decreased systolic pressure as compared to preconfinement studies.

Cardiovascular deconditioning in the presence of normal G-force application can be sufficiently marked that influences of G force diminution or absence of vertical G forces cannot be determined without adequate consideration of the influence of physical inactivity. Current and previous immobilization studies may reflect simple cardiovascular deconditioning as opposed to simulated weightlessness or absent vertical G.

Chamber work, or activities in simulated space vehicles, or actual recent manned space flights impose the problem of physical inactivity and deconditioning which make it more difficult to learn the real effects of weightlessness, changes in gaseous environment, changes in barometric pressure, or other environmental factors. Studies in these areas should include evaluation of the influence of physical deconditioning.

At the time of this writing there are no uncomplicated studies reported that clearly demonstrate that weightlessness creates an adverse effect on the circulatory system. This includes the observations of manned space flights for the Mercury Project.

The importance of cardiovascular deconditioning of a significant degree occurring while subjects are in the upright position, as well as in subjects at bedrest, has an important medical application. It suggests that, whether patients are at bedrest or in a chair, the important question is the amount of physical activity they are getting. Further attention needs to be given to improving physical activity above the level of simply being seated upright, when medically possible. An assessment of the problem of physical inactivity is an important requirement in medical management.

134. Lamb, L. E. and P. M. Stevens. Influence of lower body negative pressure on the level of hydration during bedrest. *Aerospace Medicine* 36:1145-1151, 1965.

Purpose: To determine the effect of lower body negative pressure on the level of hydration on four subjects during 22 days bedrest.

Authors' abstract: In four subjects, bedrest was used to induce recumbency diuresis. This was manifested by a decrease in fluid balance, body weight, and plasma volume accompanied with an increase in hematocrit. After the changes from bedrest had occurred, the use of LBNP over a 2-day period resulted in rehydration manifested by an increase in fluid balance. body weight, and plasma volume, accompanied with a decrease in hematocrit. The use of LBNP is an effective means to restore hydration after recumbency diuresis has occurred. This has important applications to manned space flight when it is desirable to maintain the level of hydration.

135. Lamb, L. E., P. M. Stevens, and R. L. Johnson. Hypokinesia secondary to chair rest from 4 to 10 days. *Aerospace Medicine* 36:775-763, 1965.

Authors' summary: The effects of inactivity during chair rest for periods of 4 days, 6 days, 8 days, and 10 days were studied. Despite the presence of body weight and the dependent position of the lower extremities, deconditioning occurred. The average decrease in total blood volume after 10 days was slightly greater than the average noted after 11 days of bedrest. The average decrease in red cell mass was similar to that observed after 11 days of bedrest. Orthostatic tolerance and exercise tolerance were progressively dininished with longer periods of chair rest. This study demonstrates that confinement resulting in muscular inactivity causes deconditioning even when normal gravitational factors cause body weight and increased hydrostatic pressure below the diaphragm. For this reason, deconditioning during manned space flight may be markedly influenced by confinement with restricted body movement, independent of what influence weightlessness may have on its development.

136. Larsen, W. E., N. M. McFadden, and M. Sadoff. Effects of sustained acceleration. Coriolis acceleration and bedrest on precision psychomotor control performance. *Aerospace Medical Association Preprints*, 1969, pp. 206-207.

Purpose: To determine the effects of prolonged bedrest on psychomotor performance during acceleration.

Authors' summary: Moderate sustained EBI accelerations of 6 G resulted in increases in critical time constant of 15 to 30 msec, most of which is attributable to increases in the subjects' effective time delay. Mild vestibular disturbance due to Coriolis accelerations at 2 G EBI accelerations resulted in further increases of 10 to 25 msec in the subjects' effective time delay. Short-term bedrest studies indicated no significant decreases in performance; in fact, performance tended to improve slightly during the bedrest period.

137. Leach, C. S., P. C. Johnson, and T. B. Driscoll. Effects of bedrest and centrifugation of humans on serum thyroid function tests. *Aerospace Medicine* 43:400-402, 1972.

Authors' abstract: Changes in plasma volume and protein concentration have been reported when normal subjects are bedrested or centrifuged. Since thyroid hormones are transported by specific plasma proteins, each of these procedures could be expected to change plasma levels of these hormones. In this study centrifugation of normal healthy human subjects produced an increased concentration of total protein and albumin. When these same subjects were bedrested for 6 days, no change in total protein, albumin, or thyroxine-binding globulin were found, although there was an 8-percent decrease in plasma volume. Centrifugation and, to a lesser extent, bedrest produced changes in serum T-4 levels and the T-3 test results. The direction of these changes (decreased percent T-3 values and increased T-4 levels) indicate that these two situations produce an increased plasma concentration of thyroxine-binding sites.

138. Leverett, S. D., Jr., S. J. Shubrooks, and W. Shumate. Some effects of space shuttle $+G_Z$ reentry profiles on human subjects. Aerospace Medical Association Preprints, 1971, pp. 90-91.

Purpose: To investigate $+G_Z$ tolerance to a proposed space shuttle reentry acceleration profile in bedrested men.

Procedure and methods: Nine men (20 to 36 yr), all experienced centrifuge subjects, were exposed to a normal shuttle reentry profile of a buildup to a peak of $+2.5G_Z$ at an onset rate of 1.8 G/min and hold at 2.5 G for 370 sec, then decelerate to 0.5 G at 1,8 G/min, and then a final increase to $+2.5\ G_Z$, after 1 day and 7 days of bedrest. Preliminary acceleration runs were conducted at +2.5, 3.0, 3.5, and 4.0 G_Z with an onset rate of 1 G/min and held at these plateau levels for 370 sec.

Results: The number of subjects that completed the predetermined run times listed above were:

	2.5G	3.0G	3.5G	4.0G	4.5G
Control	9 (370 sec)	8	4	2	2 (103 sec)
1-day bedrest	9 (370 sec)	7	4	1	1 (51 sec)
7-day bedrest	7 (312 sec)	5	2	1	0 (17 sec)

No significant difference was noted in absolute heart rates at the "stop" point for each subject following 1-day and 7-day bedrest compared with the same point in the control runs. Following 1-day bedrest, the mean heart rate (range 114-185 beats/min) was 145 beats/min, after 7 days bedrest it was 142 beats/min (range 92-184 beats/min), and it was 141 beats/min in the control period.

Authors' conclusions: If the space shuttle reenters in a nominal profile, it is apparent that a 1-day turnaround time in the unprotected state will not compromise the operator's visual or physiological responses. If the turnaround time is 7 days or longer, then a relaxed operator may have some visual symptoms leading to a total loss of vision. A standard anti-G suit/valve installation would protect the operator during the reentry G loadings.

139. Levy, G. Effect of bedrest on distribution and elimination of drugs. *Journal of Pharmacological Science* 56:928-929, 1967.

Purpose: To investigate drug kinetics during bedrest.

Results: The fraction of the administered dose excreted unchanged and the renal clearance of benzylpenicillin were significantly increased during bedrest.

Conclusions: The observed changes in drug kinetics during bedrest may be due to the higher metabolic rate of ambulatory subjects and the marked circulatory and plasma volume differences found in upright and recumbent subjects. It appears that comparative pharmacokinetic studies on sick, bedridden patients and healthy controls require that the latter be in bed also.

140. Lipman, R. L., P. Raskin, T. Love, J. Triebwasser, F. R. Lecocq, and J. J. Schnure. Glucose intolerance during decreased physical activity in man. *Diabetes* 21:101-107, 1972.

Authors' abstract: Impaired glucose tolerance is a well-documented consequence of absolute bedrest in man. Previous studies have shown a decrease in forearm glucose uptake during intravenous glucose infusion after 14 days of bedrest. Bedrest is associated not only with physical inactivity but with a change in gravitational vector. This study was designed to examine the individual contributions of these factors to the glucose intoleranc of bedrest. Thus, glucose tolerance tests were carried out in exercising subjects at bedrest and in rhesus monkeys immobilized in the vertical plane. Exercise in man improved glucose tolerance during bedrest, and vertically immobilized monkeys demonstrated significant glucose intolerance. It is concluded that the glucose intolerance of bedrest is a function of the decrease in physical activity.

141. Lipman, R. L., J. J. Schnure, E. M. Bradley, and F. R. Lecocq. Impairment of peripheral glucose utilization in normal subjects by prolonged bedrest. *Journal of Laboratory and Clinical Medicine* 76:221-230, 1970.

Purpose: To quantitate peripheral glucose uptake in man maintained at absolute bedrest for 14 days.

Authors' summary: The effects of 2 weeks of absolute bedrest on arteriovenous glucose difference, forearm blood flow, and peripheral glucose uptake were studied in nine subjects. A 180-min infusion of 20-percent glucose solution was administered during a control period of normal activity, on the 14th day of absolute bedrest and on the 7th or 14th day of post-bedrest recovery. Venous glucose was recorded continuously by an AutoAnalyzer. Arterial glucose, serum immunoreactive insulin (IRI), and forearm blood flow were measured. Glucose loads were varied during the bedrest and recovery infusions to match the venous glucose concentrations obtained during the control period for each subject and thus achieve similar insulinogenic stimuli between periods. While there were no significant differences in fasting preinfusion arteriovenous glucose differences or preinfusion peripheral glucose uptakes, there were significant decreases in peripheral glucose uptake during the bedrest and the 7-day-recovery glucose infusions as compared to the control and the 14-day-recovery infusions. There was a significant decrease in the mean glucose load needed to produce a comparable venous glucose curve during the bedrest as compared to the control infusion. Mean serum immunoreactive insulin concentrations were comparable during each of the three infusions. The glucose intolerance of bedrest is due, in part, to an impairment of peripheral glucose uptake which is not the result of insulin deficiency or insulin antagonists but appears to be a cellular alteration.

142. Lipman, R., F. Ulvedal, E. Bradley, and F. Lecocq. Inhibition of peripheral glucose utilization by bedrest. *Physiologist* 12:285, 1969.

Authors' abstract: Although many investigators have reported impaired glucose tolerance as a consequence of bedrest (B), there are no published data which permit a physiologic interpretation of this defect. The current study details the effects of 2 weeks of B on forearm arterial-venous glucose difference (A-V) with a simultaneous forearm blood flows (F) in 10 normal subjects fed a 380-gm carbohydrated diet. A constant 180-min intravenous infusion of glucose solution was administered twice during a 2-week control (C), on the 14th day of B, and on the 7th day of recovery (R). Venous glucose from the contralateral arm was recorded continuously and arterial glucose, serum insulin, and forearm F were measured every 10 min. Glucose loads were varied during B and R to match venous glucose levels achieved during C. Whereas fasting A-V and F were similar during C, B, and R, significant differences were obtained in mean glucose loads, A-V and (A-V) x F during glucose infusions comparing C to B and C to R.

Glucose Load (gm)		A-V (mgm percent)		(A-V) x F (mgm/min)	
$\bar{X}$	±SEM	$\bar{X}$	±SEM	$\bar{X}$	±SEM
C 165.3	9.2	C 50.6	4.0	C 0.92	0.09
B 84.3	10.1	B 19.1	2.1	B .53	.06
R 106.5	11.2	R 26.8	2.5	R .51	.05

In conclusion, the reported glucose intolerance of bedrest is in large part the result of inhibition of peripheral glucose utilization. It is suggested that this is due to local changes rather than hormonal or circulatory adaptation to bedrest.

143. Lipman, R. L., F. Ulvedal, J. J. Schnure, E. M. Bradley, and F. R. Lecocq. Gluco-regulatory hormone response to 2-deoxy-d-glucose infusion in normal subjects at bedrest. *Metabolism* 19:980-987, 1970.

Purpose: To further evaluate endocrine function during 14 days bedrest with emphasis on the effect of the glucose analogue 2-deoxy-d-glucose (2-DG) on pituitary and adrenal reserve.

Procedure and methods: Eight normal males, 18 to 21 yr, were used as subjects. They had normal oral glucose tolerance curves and had negative family histories for diabetes mellitus. The subjects underwent a 5-week ambulatory control period, 2 weeks of bedrest followed by a 10-day recovery period. They were fed 3000 kcal/day, of which 260 gm were carbohydrates.

Results:

Preinfusion plasma glucose concentrations were significantly higher during bedrest (96.9 ±2.7 mg/100 ml) compared with mean control values (89.9 ±1.2 mg/100 ml). In all cases there were significant rises in plasma glucose concentrations following 2-DG infusion.

Mean basal free fatty acid concentrations were not significantly different comparing control, bedrest, and recovery values, but were uniformly elevated following 2-DG.

Plasma cortisol and insulin concentrations were not significantly different during the three periods before or after 2-DG infusion with the exception of cortisol at 105 min.

Mean preinfusion growth hormone concentrations were lower during bedrest compared with control values. Growth hormone was elevated significantly following 2-DG.

There were no changes in basal urinary epinephrine excretion rates when comparing control and bedrest values. During bedrest, basal urinary epinephrine excretion was significantly less increased during 2-DG infusions.

Authors' conclusions: The reduced growth hormone response to 2-DG during bedrest suggests a reduction in pituitary growth hormone reserve. Bedrest does not affect basal growth hormone levels. Despite the diminished cortisol, epinephrine, and growth hormone responses following 2-DG infusion, there was no difference in plasma glucose concentration following the infusion done during bedrest.

144. Lobban, M. C. and B. E. Tredre. Renal diurnal rhythms in human subjects during bedrest and limited activity. *Journal of Physiology (London)* 171:26-27, 1964.

Purpose: To examine the affect of bedrest and limited activity on the renal diurnal rhythms in man.

Procedure and methods: Thirty-two miners, all suffering from a minor degree of pneumoconiosis, were observed after admission to a sanatorium. None had any history of renal disorder. For all subjects a week of complete bedrest was followed by a gradual reduction in the daily rest periods and an increase in physical activity. In each subject, urine samples were collected at frequent intervals over a 50-hr period on three occasions (i) during the first week of complete bedrest, (ii) during the sixth week, when rest periods alternated with very light physical activity, and (iii) during the twelfth week, when no rest periods occurred during the day and two daily walks of 3 miles were taken.

Results: The diurnal rhythms of renal excretion of water, potassium, sodium, and chloride were at all times normal in phase but were somewhat low in amplitude. The pattern of potassium excretion appeared least affected. The amplitudes of the excretory rhythms of all the urinary constituents were greater during the period of moderate daily activity than when the subjects were on bedrest or on very limited activity; but in the majority of subjects, excretory patterns showed far more disturbance during the period of limited activity than they did during bedrest.

Conclusions: It would appear that the amplitude of the renal diurnal rhythms in man is reduced during and after prolonged periods of severe limitation of activity.

145. Lockwood, D. R., J. M. Vogel, D. A. Hantman, C. L. Donaldson, and S. B. Hulley. The use of calcium (Ca) and phosphate supplementation to prevent bone mineral loss during prolonged bedrest (BR). *Clinical Research* 20:239, 1972.

Authors' abstract: Mineral supplements (Rx) were used in an attempt to prevent the negative Ca and phosphorus (P) balances and loss of bone mineral which occur during BR. Five healthy Caucasian men, aged 20-27 yr, were studied on metabolic balance for 24 weeks, including 17 weeks of continuous BR. The diet contained 1027 mg Ca and 1656 mg P/day; during BR, three of the five subjects received daily Rx of 1315 mg Ca (as lactate) and 1419 mg P (as potassium phosphate). Mean balance results are expressed as change from baseline in mg/day. Bone mineral was assessed by gamma-ray absorptiometry; data for the last week of each period are expressed as percent of mean baseline.

	Weeks BR	Balance		Bone Mineral	
		Ca	P	Calcaneus	Tibia
Rx	1-11	+ 97	+ 94	100	101
	12-15	- 17	- 3	94	99
	16-17	- 92	- 49	94	96
No	1-11	-148	-176	92	89
Rx	12-17	-182	-182	87	90

Rx prevented negative Ca and P balance during the first weeks of BR. During the final 6 weeks of BR, all three treated subjects developed negative Ca and P balances, approaching the levels of the controls. Loss of mineral from the calcaneus and the distal tibia was usually diminished by Rx.

The data suggest that Rx prevents disuse osteopenia for 2-3 months, but there is a subsequent escape from this effect. If these results are applicable to more common types of osteopenia, long-term use of Rx is unlikely to have substantial prophylactic or therapeutic effects.

146. Lorentsen, E., C. Eika, and H. C. Godal. Coagulation studies in chronically bedridden patients. *Acta Medica Scandinavica* 195:79-80, 1974.

Abstract: Twelve patients (67 to 97 yr) had been confined to bed for 1.5 to 8 yr. They all suffered from cerebral atherosclerosis with dimentia of different degree. Analyses of the platelet count, normotest, thrombotest, thromboplastin time, fibrinogen concentration, antithrombin III, Factor V, thrombin time, and the ethanol test were within normal limits. These results suggest that slowing of the circulation due to bedrest as the only precipitating factor is inadequate to induce clinically significant thrombosis or signs of coagulopathy. Since the survival of platelets in healthy subjects is not affected by bedrest and repeated animal experiments have shown that stasis alone fails to induce blood clotting, it appears that additional factors, such as hypercoagulability, are probably required to initiate thrombogenesis.

147. Lutwak, L. and G. D. Whedon. The effect of physical conditioning on glucose tolerance. *Clinical Research* 7:143-144, 1959.

Authors' abstract: Increased glucose utilization has been shown to occur during acute exercise, and chronic diseases associated with physical inactivity have been shown to be associated with decreased utilization of orally administered glucose. The subject of the present report is the production of the latter phenomenon and its reversibility by physical conditioing in normal individuals. Ten normal young adults, six females and four males, receiving diets containing 200-400 gm of carbohydrate a day and at least 2400 calories, were placed at complete bedrest for 1 to 3 weeks. Subsequently, they were placed on a regimen of increasing exercise for 2 to 6 weeks, based on treadmill walking in addition to ad libitum gymnasium activities. Intravenous glucose tolerance tests were performed at rest at intervals prior to and during the bedrest phase and during the activity period. Glucose utilization coefficients were calculated according to the method of Amatuzio et al. Although a wide interindividual variability of glucose utilization was observed, in all the subjects complete inactivity produced a marked decrease in glucose utilization within the first week of bedrest with values in the diabetic range. Within a week following institution of the program of physical reconditioning, the utilization returned to baseline values, with some individuals showing utilizations far above normal. Chronic activity, or physical conditioining results in increased efficiency of the utilization of glucose. Conversely, enforced bedrest leads to impaired glucose utilization.

148. Lynch, T. N., R. L. Jensen, P. M. Stevens, R. L. Johnson, and L. E. Lamb. Metabolic effects of prolonged bedrest: their modification by simulated altitude. *Aerospace Medicine* 38:10-20,1967.

Authors' abstract: Metabolic studies were performed on 44 healthy men before and during bedrest at ground level or at simulated altitudes of 10,000 or 12,000 ft. Simple bedrest brought loss of calcium, phosphorous, nitrogen, sodium, and chloride with little change in potassium. The addition of 12,000-ft simulated altitude significantly reduced the loss of urinary calcium, phosphorus, nitrogen, sodium and chloride, and total nitrogen. The 10,000-ft simulated altitude was associated with urinary calcium losses quantitatively intermediate between the ground level and 12,000-ft groups and increased total sodium and potassium losses. The possiblity that reduced bone resorption represents one aspect of acclimatization to simulated altitude is discussed.

149. Mack, P. B. and P. L. LaChance. Effects of recumbency and space flight on bone density. *American Journal of Clinical Nutrition* 20:1194-1205, 1967.

Authors' summary: Evaluations of bone mass changes in terms of calcium hydroxyapatite equivalency have been made for the central section of the os calcis and for hand phalanx 5-2 of man participating in seven bedrest units consisting of an equilibration period, a 14-day-bedrest period, and a reconditioning period, with the level of calcium intake during bedrest ranging from 300 to 2000 mg daily. The same type of bone mass determinations was made on the crews of the Gemini IV, V, and VII missions. The method of radiographic bone densitometry was used to evaluate skeletal changes in both groups of subjects.

A significant negative coefficient of correlation was found between bone mass losses in the central section of the os calcis and the mean levels of daily calcium intake after 14 days of horizontal bedrest. Significant positive correlations were found between intake of dietary calcium and outgo of urinary and fecal calcium.

In four bedrest units in which the same level of dietary calcium was fed in the pre-bedrest ambulatory equilibration period as during the bedrest phase, the urinary and the combined urinary and fecal calcium output during bedrest surpassed that during ambulation by significant differences throughout.

With respect to the three groups of astronauts, the duration of the orbital flight evidently was not the sole factor in losses of bone mass since the astronauts engaged in the longest space flight experienced the lowest negative changes in bone density.

Although mean daily calcium consumption was found to be related negatively to bone density losses in subjects during bedrest, the same could not be stated unequivocally concerning astronauts during space flight with the evidence now in hand because of uncontrolled variables such as stress and dietary factors in addition to calcium. Also, the exercise program introduced into the Gemini VII flight imposed a new variable which contributed to the reduction of bone mass in the os calcis as supported by ground-based trials with bedrest subjects.

Because of the small number of subjects in the space flight study to date, further data will need to be acquired from future flights in order to understand the interrelationships more fully.

150. Mack, P. B. and K. B. Montgomery. Study of nitrogen balance and creatine and creatinine excretion during recumbency and ambulation of five young adult human males. *Aerospace Medicine* 44(7):739-746, 1973.

Author's summary: Five male university students participated in a study conducted at the Texas Women's University Research Institute. The study lasted for 97 days and included two 14-day bedrest periods. A careful record was kept of the urinary nitrogen, fecal nitrogen, urinary creatine, and urinary creatinine excreted daily by each subject. The average excretion values for all subjects were within normal range.

Urinary nitrogen excretion for all subjects increased during bedrest no. 1 as compared to the pre-bedrest period, with a statistical significance ($p < 0.01$) between the two periods. The highest mean value among all subjects for urinary nitrogen excretion during the entire study was obtained during bedrest no. 2, when the overall average excretion was 12.24 gm/24hr. This mean value for all subjects for bedrest no. 2 was found to be highly significant ($p < 0.001$) when it was compared with the value for the pre-bedrest period.

Excretion values for fecal nitrogen varied only slightly between periods when statistical comparisons were made between the values for the various periods of the study. All subjects showed an increase in urinary nitrogen during the bedrest periods and a decrease in fecal nitrogen during both bedrest periods.

All subjects remained in positive nitrogen balance throughout the study. Of the total nitrogen excreted, 96.6 percent was found in the urine and 3.4 percent in the feces.

All five subjects exhibited a generally minor weight decrease during bedrest no. 1. Two subjects lost weight during bedrest no. 2. Three subjects at the end of the study were lighter in weight than they had been upon entering this investigation.

During bedrest no. 1, the average excretion of urinary creatine for all subjects was 110.0 mg daily as compared with 80.0 mg daily during the pre-bedrest period. This had a statistical significance ($p < 0.05$). During bedrest no. 2 the excretion of creatine fell to an average of 38.0 mg/24hr. This drastic decrease in creatine excretion was found to be highly significant when compared to the excretion values for bedrest no. 1.

The mean creatinine excretions for all subjects during the different periods of the study showed that very little overall change took place.

Statistical comparisons of urinary creatine and creatinine between pairs of the different periods of the study are outlined in Tables V and VI. The most significant finding in this study was the greater excretion of creatine during the first bedrest as compared to the second bedrest when the calcium intake dropped from 800 mg daily to 300 mg/day. This was a consistent finding for all subjects.

The results of this study suggest a possible connection between dietary calcium and creatine excretion. Since no studies were found in the literature to substantiate this finding, it is felt that further investigation as to the relationship between low dietary calcium intake and low creatine excretion is indicated.

151. Makarov, G. F. Effect of cyclic atmospheric changes on human basal metabolism during prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 4:64-67, 1970.

Author's abstract: A study was made of the effect of cyclic atmospheric changes on human basal metabolism during prolonged hypokinesia. Two healthy test subjects were confined to an altitude chamber for 35 days. The experiment consisted of 5 cycles lasting 7 days each. On the third day, the atmosphere was hypoxic ($PO_2 = 110 \pm 5$ mm Hg); on the fourth day it was hypoxic ($PO_2 = 110 \pm 5$ mm Hg) and hypercapnic ($PO_2 = 15 \pm 3$ mm Hg); on the seventh day it was hyperoxic ($PO_2 = 320 \pm 10$ mm Hg); on the remaining days a normal atmosphere was maintained. The results of the preliminary experiments suggest that cyclic alternations of hypoxia and hypoxia combined with hypercapnia may give a stimulating effect which compensates for a hypokinesia-induced decline in metabolism.

152. Marishchuk, V. L., T. T. Dzhamgarov, Yu. K. Dem'yanenko, V. P. Stupnitskiy, and B. S. Khvoynov. Stability of psychic functions during prolonged confinement to bed. *Problemy Kosmicheskoy Biologii* 13:175-182, 1969.

Purpose: to evaluate the stability of the psychic function during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' summary: Undesirable changes in the psychic functions were manifested to a lesser degree than were vegetative shifts. For the most part, the subjects retained operational efficiency and matched their original scores or even improved on them as a result of training in tests that characterize memory, the stability, distribution, and transfer of attention, sensomotor reactions, accuracy of time-interval judgment, mentation efficiency, etc. Sometimes the minor changes observed had an initial tendency toward deterioration, with a subsequent improvement of the indicators on the function-mobilization pattern, resembling the "anxiety reaction" to a state of stress. Such changes were particularly distinct during some of the periods when psychopharmaceuticals were being given. The detrimental changes were less frequent in the groups who performed physical exercises. The decrease in emotional stability and the increase in the numbers of errors can be explained by preferential weakening of the inhibitory process.

153. Maslov, I. A. Mental states during prolonged hypokinesia. *Zhurnal Nevropatologii i Psikhiatrii* 68:1031-1034, 1968.

Purpose: To investigate mental changes in subjects duirng prolonged bedrest.

Procedure and methods: Six healthy men (23 to 36 yr) were confined to bed under ordinary hospital conditions for 62 days.

Results:

Days 1-2: The state of the subjects could be characterized by high spirits; there was always music, singing, jokes, and laughter. The subjects said their mood was good, excellent, and fine. Nevertheless, several subjects exhibited agitation, with a slight shade of fear and uncertainty.

Days 3-6: A period of physical discomfort. The subjects complained of unpleasant feelings, pains in various parts of their body, and they said they were uncomfortable in bed and they often turned over trying to find the most comfortable position. By this time the novelty of the situation had disappeared and their mood was mainly determined by the degree of physical discomfort.

Days 7-20: A period of adaptation to the experimental conditions. Their unpleasant physical feelings gradually disappeared and the subjects could lie for hours in one position without feeling the need to change it. Their mental states were even and calm.

Days 21-35: The period of beginning asthenic symptoms. The subjects complained that it was becoming difficult to lie down, they wanted to move, they were getting tired of the monotony, the sameness of the situation, things were the same day after day, there was nothing new; some, jokingly, said that only now did they realize how good it had been when they were "alive," when the present limitations did not exist. Symptoms of irritability and intolerance appeared. The subjects less readily entered into conversation with their neighbors, sleep in the majority became shallow, some dreamed more often.

Days 36-62: Gradually symptoms of asthenia increased and by the end of the experiment the subjects had become irritable, touchy, and capricious: they reacted violently to every little thing infringing on their interests. They themselves often correctly evaluated their state, saying that now everything irritated them: for example, that they were wakened early, they did not get what they asked for immediately, they were annoyed by certain ("unsympathetic") staff members. Conflicts developed more often with their neighbors and especially with the experimentors. Sleep disturbances were aggravated.

Here are some typical complaints of this period: time passes slowly, you don't know what to do with yourself; the frequent examinations (even the very slight ones) are annoying, especially those not stipulated on the schedule; it is difficult to concentrate on studies (some of the subjects were students), nothing stays in your head. Some individuals declared that sometimes they felt like "doing" something; often these intentions were carried out: for example, somebody all of a sudden began to cry in a loud monotone: "a-a-a." The cry was heard throughout the section. Some noted that they became "terribly irritable," sometimes they wanted to "throw something at somebody, to tear something to pieces." One of the subjects complained that at times, especially toward evening, he "gets the blues," he frets, he would like to be home.

These mental changes were typical of all subjects, although the degree of severity differed. In some there were also other disturbances evidently connected with characterological features. For example, a premorbidly slightly hypochondriac subject often complained of general indisposition, some kind of indefinable feelings in his head: his head was heavy, it felt like things were coming apart inside, when he closed his eyes it felt as if his head were being thrown to the side. Two subjects with traits of mental infantilism showed more pronounced capriciousness and stubbornness, there were elements of puerilism in their behavior. And, on the other hand, in subjects with no premorbid characterological deviations, mental changes were less pronounced.

In the very last days of the experiment, all subjects were in a good mood (elation) and talkative. The subject of conversation was the impending end of the experiment. In the majority, sleep disorders were increased. Several days before the end of the test it was explained that the experiment would be prolonged 2 days. In all subjects this caused a reaction of resentment, they unanimously stated that if from the very start it had been planned that the experiment would last for 62 days instead of 60, it wouldn't have mattered; now the additional 2 days seemed very long. This indicates the important role of psychological factors such as building up to the end of the test.

Immediately after the experiment ended, the subjects were excited, uninhibited, gay. They continuously walked through the section, looked out of the windows, tried to talk to everybody. We must note that in subjects who had previously taken part in similar experiments, this reaction was less pronounced. Noted on the first days after the end of the test were general weakness, poor tolerance of physical loads, and reduced orthostatic stability.

Thus, the clinical picture, developing primarily in the second half of the experiment, corresponds to the typical neurasthenic syndrome. This is experimental neurosis in the form of neurasthenia. Its characteristics were a predominance of hypersthenic symptoms (irritability, explosiveness, activity) and comparatively mild symptoms of asthenia proper (debility, exhaustion, adynamia).

Mental changes were slightly more pronounced in subjects not performing physical exercises; however, the small size of the group and the differences in premorbid features do not allow definite conclusions about the role of physical exercises.

154. McCally, M., T. E. Piemme, and R. H. Murray. Tilt table responses of human subjects following application of lower body negative pressure. *Aerospace Medicine* 37:1247-1249, 1966.

Authors' abstract: Orthostatic tachycardia and hypotension are known consequences of bedrest in normal subjects. This response is felt to follow from the reduction in plasma volume accompanying the salt and water diuresis of recumbency. Similar effects are felt to result from zero gravity during manned space flight. Lower body negative pressure (LBNP) has been suggested as a countermeasure to such adverse effects of

weightlessness. Tilt-table test responses were measured in six subjects after exposure to two conditions of LBNP. Six hours of intermittent (1-min on, 1-min off) LBNP (55 mm Hg) prevents the orthostatic tachycardia of 6 hr of bedrest. A continuous 90-min LBNP (30 mm Hg) exposure improves the tilt response to better than control values. These data support the proposal that LBNP may be useful in maintaining the orthostatic tolerance of confined and weightless astronauts.

155. McCally, M., S. A. Pohl, and P. A. Samson, Jr. Relative effectiveness of selected space flight deconditioning countermeasures. *Aerospace Medicine* 39:722-734, 1968.

Authors' abstract: Head-out neutral temperature (34°C) water immersion of human subjects produces diuresis, plasma volume contraction, decreased urinary norepinephrine excretion, and subsequent orthostatic intolerance. Similar responses have been reported after prolonged manned space flight. Six protective techniques or countermeasures, including (1) four extremity venous tourniquets or cuffs, (2) an elastic leotard, (3) antidiuretic hormone (ADH) injection, and (4) cold immersion (30°-31°C), were assayed for their ability to alter or prevent these immersion responses. Chair rest, bedrest, and bedrest with lower body negative pressure (LBNP) were studied as non-immersion controls. Venous blood and urine were collected in six subjects every 2 hr during each 8-hr exposure. The elastic leotard donned after immersion, just prior to tilt, was the most effective measure tested and restored tilt-table responses to control level ($p < 0.01$). Four extremity venous tourniquets, inflated 2 min on and 4 min off, offered no protection but in a 1-min on and 1-min off cycle, significantly ($p < 0.05$) increased urinary norepinephrine excretion and decreased the the maximum heart rate response to the post-immersion tilt. Cold significantly increased urinary norepinephrine excretion during immersion but did not prevent post-immersion orthostatic tachycardia. Antidiuretic hormone administration prevented the immersion diuresis but was without effect on subsequent tilt-table tolerance. These observations may be pertinent to the prevention of the orthostatic intolerance seen after prolonged manned space flight.

156. McDonald, C. D., G. E. Burch, and J. J. Walsh. Alcoholic cardiomyopathy managed with prolonged bedrest. *Annals of Internal Medicine* 74:681-691, 1971.

Authors' abstract: The influence of complete prolonged bedrest on the clinical course of 48 patients with alcoholic cardiomyopathy was studied. Heart size returned to normal with bedrest in 21 (57 percent) of the 37 patients who cooperated fully, decreased considerably in 11 (30 percent), and did not change in 5 (13 percent). Of the 21 patients whose heart size returned to normal, 13 (62 percent) are presently living, 9 (43 percent) with normal heart size. Of the other 27 patients, only 10 (37 percent) are known to be presently alive, none with normal heart size. Response to bedrest therapy and long-term prognosis apparently are affected by duration and severity of the heart disease at the time bedrest is instituted. Unfortunately, the ultimate prognosis in many patients is poor because of delay in diagnosis, unwillingness to accept prolonged bedrest therapy, inability to refrain from alcohol consumption, inadequate nutrition, and excessive physical activity.

157. McDonald, J. K., T. J. Reilly, B. B. Zeitman, J. E. Greenleaf, H. Sandler, and S. Ellis. Effect of prolonged bedrest and $+G_Z$ centrifugation on blood fibrinolytic activity in males and females and its possible use as a measure of vascular deconditioning. Aerospace Medical Association Preprints, 1974, pp. 167-168.

Purpose: To correlate blood levels of plasminogen activator following $+G_Z$ centrifugation with $+G_Z$ tolerance and to examine the possiblity of utilizing such a response as a possible index of tissue hypoxia and/or vascular deconditioning.

Procedure and methods: Data were obtained from 19 subjects studied in three groups to compare various countermeasures such as isotonic and isometric exercise with periods of absolute bedrest. Group I (males, 21-23 yr) performed moderate isotonic exercise in the supine position with a bicycle ergometer. Group II (males, 19-22 yr) underwent three consecutive 14-day periods of bedrest, separated from each other by 21-day periods of ambulatory recovery. Group III (females, 23-24 yr) underwent 14 days of bedrest without exercise. Tolerance to three levels of $+G_Z$ acceleration (2G, 3G, and 4G) for groups I and II was determined immediately before and on the last day of each bedrest period. Tolerance to $+3G_Z$ acceleration for group III was determined and compared with control values. Blood samples drawn before and 5 min after centrifugation were used to measure the plasminogen activator content of the plasma (euglobulin) and the latter blood samples were used for fibrinolysin studies.

Results: The increase in $+G_Z$-induced fibrinolysis occurred in spite of the various contermeasures that were employed. The response was 140 percent ($p < 0.005$) greater after bedrest with isometric exercise, 105 percent ($p < 0.005$) greater after bedrest with isotonic exercise, and 83 percent ($p < 0.025$) greater after bedrest without exercise.

Both males and females showed highly significant mean fibrinolytic responses to $+G_Z$ centrifugation. The males showed a response after bedrest ($\Delta = +254$ mm^2) that was significantly greater ($p = 0.05$) than the response before bedrest ($\Delta = +147$ mm^2). The females, on the other hand, gave a strong fibrinolytic response both before and after bedrest. The mean fibrinolytic response after bedrest ($\Delta = +265$ mm^2) was not significantly greater than the mean response before bedrest ($\Delta = +244$ mm^2).

The results show that 14 days of bedrest raised the mean basal level of fibrinolytic activity in females from 212 to 285 mm^2, an increase of 35 percent ($p = 0.01$). The apparent increase in the mean basal level for the males (157 to 194 mm^2) was not statistically significant.

Conclusions: It is tentatively concluded that bedrest deconditioning produced changes in the vascular integrity that led to a more active secretion of plasminogen activator in response to hypoxia. Consequently, an elevated fibrinolytic response to a $+G_Z$ stress following bedrest is considered to be a possible manifestation and potential measure of this deconditioning phenomenon.

158. Meehan, J. P., J. P. Henry, S. Brunjes, and H. deVries. Investigation to determine the effects of long-term bedrest on G-tolerance and on psychomotor performance. Final Report, Contract NAS9-3500, Department of Physiology, University of Southern California, Los Angeles. Sept. 1966.

Authors' abstract: Fourteen young men were confined to bed for 28 days. They were randomly divided into three subject groups of 5, 5, and 4 individuals. One group exercised, another did pressure breathing, and the third did both. Each subject was exposed to a reentry acceleration profile in the $-G_x$ position while performing a three-dimensional tracking task prior to the bedrest and at the conclusion of the bedrest. Tilt-table tolerance and blood volumes were determined in a similar sequence.

Cardiovascular deconditioning manifested by plasma volume decrements of 20 percent and decreased tolerance to passive tilting resulted in all subjects and was not differentially affected by the exercise, pressure breathing, or the combination maneuvers.

Performance on the tracking task during acceleration was not affected by the cardiovascular deconditioning.

159. Menninger, R. P., R. C. Mains, F. W. Zechman, and T. A. Piemme. Effect of two weeks bedrest on venous pooling in the lower limbs. *Aerospace Medicine* 40:1323-1326, 1969.

Authors' abstract: Greater leg circumference increase with tilt following weightlessness suggests that increased venous distensibility may contribute to postflight orthostatic intolerance. The present study was conducted to determine by more direct measurements the effect of inactivity (2 weeks bedrest) on the pressure-volume characteristics of the legs. Lower body negative pressure (LBNP) of a magnitude (−40 mm Hg) known to produce blood volume shifts similar to those occurring with tilt was applied to two subjects before and at the end of the bedrest period. Leg volume changes were measured directly at 1, 3, and 5 min using whole leg water plethysmographs located in the LBNP chamber. The measured volume changes suggest that venous distensibility was not increased by 2-week bedrest. The characteristic increase in heart rate elicited by LBNP was greater following bedrest as anticipated. In view of the apparent inconsistency between previous circumference measurements and the present plethysmographic observations, additional studies are needed to delineate the importance of changes in venous distensibility in "cardiovascular deconditioning."

160. Mikhasev, M. I., V. I. Sokolkov, and M. A. Tikhonov. Certain peculiarities of external respiration and gas exchange during prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:72-78, 1969.

Purpose: To investigate the effect of prolonged bedrest on external respiration and metabolism.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' summary: The effects of 70-day hypodynamia on the basal metabolic level, the spirographic and pneumotachymetric indicators of external respiration, oxygenation of arterial blood, bloodstream velocity, and gas exchange under standard physical load and in orthostatic tests were studied. Basal metabolism was lowered by 5-21 percent, pulmonary ventilation volume was reduced, oxygen demand in the orthostatic tests was increased, and there was a substantial decrease in the tolerance of physical load. The disturbances noted were mitigated by the use of preventive measures: medication and physical exercise.

161. Mikhaylovskiy, G. P., T. V. Benevolenskaya, T. A. Petrova, I. Ya. Yakovleva, O. I. Boykova, M. P. Kuz'min, A. A. Savilov, and S. N. Solov'yeva. The combined effect of two-month hypokinesia and radial accelerations on the cardiovascular system. *Kosmicheskaya Biologiya i Meditsina* 1:57-60, 1967.

Authors' abstract: Six healthy male test subjects were exposed to a 62-day bedrest and radial accelerations of the maximum tolerable magnitude. The bedrest reduced the strength of the muscular vessels, disturbed the ophthalmic and nasal regional circulation, and decreased the orthostatic tolerance of all the subjects. The latter was associated with some cardiovascular disorders and deterioration of circulatory mechanisms of adaptation to a physical load. The combined effect of bedrest and radial accelerations on the cardiovascular system was more distinct than the effect of accelerations alone. Physical exercises performed during bedrest yielded positive results.

162. Mikhaylovskiy, G. P., N. N. Dobronravova, M. I. Kozar', M. M. Korotayev, N. I. Tsiganova, V. M. Shilov, and I. Ya. Yakovleva. Variation in overall body tolerance during a 62-day exposure to hypokinesia and acceleration. *Kosmicheskaya Biologiya i Meditsina* 1:66-70, 1967.

Purpose: To investigate body immunological reactivity during bedrest.

Procedure and methods: Six men (22 to 36 yr) were subjected to 62 days of bedrest. Three subjects performed a group of physical exercises of increasing intensity and the other three subjects did no prescribed exercise. Caloric intake was 3000 to 3500 kcal/day. Once every 10 days, the subjects were washed with soap and hot water.

Six to 12 days before bedrest, on the lst and 18th days, and three subjects on the 50th day were subjected to transverse acceleration (11 to 16 $+G_X$) with an acceleration rate of 9 to 12 G/min. Body immunological reactivity was determined from measurements of blood properdin, neutrophil phagocytic activity, saliva lysozyme activity, and skin bactericidal function. These tests were conducted twice before bedrest, three to six times during bedrest, and one to three times during recovery.

Results: Blood properdin content dropped markedly during bedrest in the control group. Properdin content did not return to normal levels 50 days after bedrest ended. Exercise during bedrest did not appreciably affect the decline of properdin. Blood neutrophil phagocytic activity decreased significantly during bedrest. There was no appreciable decrease in phagocytic activity in the exercise group. The intensity of phagocytosis also decreased in the control group and returned to normal 15 to 19 days after bedrest.

In the control group at the end of bedrest, the lysozome titers were 5 to 8 times lower than initial levels. Lysozome titers were not restored to initial levels by the 15th day of recovery. In the control group there was a marked depressed (23 to 35 percent) skin bactericidal activity during bedrest. Physical exercise during bedrest maintained activity at control levels.

Conclusions: Physical exercise during bedrest retards or eliminates the decreased action of the immunological reactivity system.

163. Miller, P. B. Medical problems of weightlessness. *Texas State Journal of Medicine* 61:720-724, 1965.

Author's summary: The similarity between prolonged spaceflight and prolonged bedrest suggests that the adverse physiologic effects of bedrest may also develop during spaceflight. A decrease in exercise tolerance, orthostatic tolerance, muscle strength, and blood volume and an increase in urinary calcium excretion occur during prolonged bedrest. Orthostatic intolerance has been reported after American and Soviet spaceflights.

The preservation of normal postural tolerance will probably require some method of simulating hydrostatic effects of gravity on the body fluids, in addition to physical exercise. Intermittent lower body negative pressure, which provokes cardiovascular responses similar to those of standing, shows promise of maintaining postural tolerance. Until in-flight methods to protect orthostatic tolerance are perfected, the wearing of an antigravity suit should prevent postural fainting after landing from a prolonged spaceflight.

To maintain circulatory and physical endurance, vigorous exercise similar to that performed on a bicycle appears necessary. Isometric exercise should be adequate for maintaining muscle strength. No method to prevent osteoporosis and its attendant hypercalciuria has been discovered.

Certainly, no great degree of anxiety is merited concerning the adverse physiologic effects of spaceflights programmed for the next several years. With the use of successively longer flights, the accuracy of predictions concerning medical problems of prolonged spaceflight can be assessed without danger to the astronaut. In the meantime, ground-based research may develop countermeasures ready for use as soon as a specific medical problem of spaceflight is delineated.

164. Miller, P. B., B. O. Hartman, R. L. Johnson, and L. E. Lamb. Modification of the effects of two weeks of bedrest upon circulatory functions in man. *Aerospace Medicine* 35:931-939, 1964.

Purpose: To evaluate the effect of intermittent venous occlusion, bedrest with the head elevated, and in-bed exercise taken singly and in combination on orthostatic tolerance after 14 days of bedrest.

Procedure and methods: Seventy-two healthy men (17 to 23 yr) underwent a control bedrest period of 2 weeks with no remedial procedures, then a 4-week ambulatory recovery period when 12 subjects pursued normal activity, and the remaining 60 subjects underwent daily tilt-table training and physical exercise which included running, situps, pushups, straight-leg raising, somersaults, and headstands. During the following 2 weeks of bedrest, these subjects were divided into six groups of 12 men each: group A–non-preconditioned control; group B–preconditioned control; group C–intermittent venous occlusion cuffs on the extremities to 60 mm Hg for 1 min each, 5 min from 0700 to 2200 hr daily; group D–elevation of head of bed 10° during bedrest; group E–a combination of intermittent venous occlusion and an elevated bed; and group F–in-bed isometric and isotonic exercises performed about 15 min/hr for 8 hr/day. Hemoglobin and hematocrit determinations were done before and after bedrest on 42 subjects. All subjects consumed about 2400 kcal/day throughout the study.

Results:

During tilting there was a decrease in heart rate following the ambulatory training period and an increase following bedrest. Group E had better orthostatic tolerance after the second bedrest period than any other group. Syncope was 15 times more common after the first 2-week bedrest period compared with pre-bedrest values.

There was a progressive loss in body weight throughout the study: 2400 kcal/day was not sufficient caloric intake.

During bedrest there was a tendency for the resting heart rate to increase, but group E exhibited the smallest increase.

The 4-week training period seemed to improve orthostatic tolerance. There was no increased benefit on orthostatic tolerance following the in-bed exercises.

Conclusions: Physical conditioning plus intermittent tilting improves orthostatic tolerance when ambulatory. A program consisting of exercise and tilt-table training before bedrest and intermittent venous occlusion of the extremities during bedrest in a 10° head-up bed resulted in almost complete preservation of normal orthostatic tolerance.

165. Miller, P. B., R. L. Johnson, and L. E. Lamb. Effects of four weeks of absolute bedrest on circulatory functions in man. *Aerospace Medicine* 35:1194-1200, 1964.

Purpose: To study the effect of 28 days of bedrest on the circulatory system of man.

Procedure and methods: Twelve healthy men (17 to 22 yr), who had just completed basic training, participated in the study. Blood volumes were measured with I-131 3 days before bedrest on the 11th and 28th days of bedrest and in six subjects on days 2, 15, and 29 of the recovery period. Orthostatic tolerance was measured with a 90° head-up tilt for 30 min or until syncope before and after bedrest. An antigravity suit was worn during some of the tilt tests to determine its effectiveness in preventing syncope.

Results: In 12 subjects, there was an average loss of 500 ml in plasma volume after 11 days of bedrest. Red cell mass was unchanged. At the end of 28 days of bedrest, loss in total blood volume ranged from 200 to 1300 ml (average loss was 730 ml). Plasma volume loss ranged from 300 to 800 ml (mean was 550 ml). Red cell mass decreased in 8 subjects from 100 to 500 ml, was unchanged in one subject, and increased 100 ml in two subjects and 200 ml in one subject. The average loss of plasma volume after 4 weeks of bedrest was essentially unchanged from that measured after 2 days of bedrest. After 15 days of recovery, red cell mass was depressed 370 ml and plasma volume increased slightly. Four weeks after bedrest total volume and red cell mass were still depressed below control levels. After 4 weeks of bedrest, the reduction in total blood volume for the four subjects with the best orthostatic tolerance was 13.1 and 13.3 percent for the four subjects with the worst orthostatic tolerance. During 4 weeks of bedrest the average weight loss was 2.55 kg (range 0.6 to 5.8 kg); one subject gained 0.5 kg.

Conclusions: Orthostatic tolerance was not related to loss of blood volume. Syncope during tilting was more frequent after bedrest. The antigravity suit eliminated postural syncope after bedrest.

166. Miller, P. B., R. L. Johnson, and L. E. Lamb. Effects of moderate physical exercise during four weeks of bedrest on circulatory functions in man. *Aerospace Medicine* 36:1077-1082, 1965.

Purpose: To investigate the effect of isotonic exercise and pressure cuffs on the lower limbs on the course of bedrest deconditioning.

Authors' summary and conclusions: Various effects on circulatory functions of light to moderate physical exercise during 4 weeks of bedrest were studied in six healthy male volunteers. During exercise narrow cuffs inflated to 68 mm Hg were worn on the upper thighs. An identical schedule of tests was followed before and after bedrest.

An average loss of 1212 ml in total blood volume occurred during 4 weeks of bedrest. An average decrease of 672 ml in plasma volume and 539 ml in red cell mass was observed. Changes in plasma volume during and after bedrest paralleled changes characteristic of simple bedrest. In contrast to simple bedrest, the major loss of red cell mass was noted at the end of bedrest and not during ambulation following bedrest.

The mean resting heart rate for all subjects increased 15 beats/min during bedrest. Syncope on the tilt table was more frequent and orthostatic heart rates were higher after bedrest than before. The degree of postural intolerance after the bedrest conditions of this study appeared as marked as that observed after absolute bedrest.

As judged by the time required to reach a heart rate of 180 or greater and by maximal oxygen consumption, physical endurance on the treadmill was not maintained by the in-bed isotonic exercise program utilized in this study. On the basis of the heart rates and oxygen consumptions during the in-bed exercise, the circulatory system was not greatly stressed. These results do not preclude the possibility that other exercise programs would favorably influence the maintenance of orthostatic tolerance and physical work capacity during bedrest.

167. Miller, P. B. and S. D. Leverett, Jr. Tolerance to transverse ($+G_X$) and headward ($+G_Z$) acceleration after prolonged bedrest. *Aerospace Medicine* 36:13-15, 1965.

Authors' abstract: Tolerance to the transverse ($+G_X$) acceleration of a simulated Gemini reentry profile was determined before and after 4 weeks of absolute bedrest. Tolerance to headward ($+G_Z$) acceleration was studied before and after 4 weeks of absolute bedrest and 2 weeks of modified bedrest.

As judged by the degree of physical discomfort, the ability to respond to a central light, or the presence of electrocardiographic abnormalities, tolerance to $+G_X$ was unaffected by 4 weeks of absolute bedrest. In each subject studied, heart rates during peak acceleration were higher after bedrest than before.

As judged by the level of acceleration at which central vision was lost, no significant change in tolerance to headward ($+G_Z$) acceleration of rapid onset was observed after 2 weeks of modified bedrest or after 4 weeks of absolute bedrest. After each type of bedrest, the majority of the subjects had decreased tolerance to headward ($+G_Z$) acceleration of gradual onset, but the mean decrease was not statistically significant.

Mean heart rates at equivalent levels of $+G_Z$ were significantly higher after both periods of bedrest. The only arrhythmia of clinical importance noted was the appearance of bursts of premature atrial contractions during G. O. R. $+G_Z$ in one subject after 2 weeks of bedrest.

168. Moore Ede, M. C. and R. G. Burr. Circadian rhythm of urinary calcium excretion during immobilization. *Aerospace Medicine* 44:495-498, 1973.

Authors' abstract: Ten healthy subjects were studied during 2 days of normal activity and 2-4 days of strict bedrest. Urinary calcium excretion was raised during bedrest, but the increase was not uniformly distributed over each 24 hr. Instead the incremental calcium excretion showed a marked circadian rhythm with 61 percent excreted between 0900 and 1500 hr. A similar pattern of calcium excretion was seen in four immobilized patients with recent-onset traumatic paraplegia. However, two chronic paraplegics without hypercalciuria did not have such an excretory rhythm. Circadian rhythms of bone resorption appear to account for the observed rhythm of urinary calcium excretion.

169. Moore Ede, M. C., M. H. Faulkner, and B. E. Tredre. An intrinsic rhythm of urinary calcium excretion and the specific effect of bedrest on the excretory pattern. *Clinical Science* 42:433-445, 1972.

Authors' summary: The diurnal rhythms of urinary calcium excretion were studied in healthy subjects under four different regimens in which diet, activity, and posture were varied. The excretory rhythms observed were compared with those of potassium, obtained under the same conditions. When the subjects were active throughout the day and night and were either fasting or eating standard 3-hourly meals, an intrinsic calcium rhythm was isolated with maximum amounts excreted between 0600 and 0900 hr. Continuous supine bedrest was found to have a specific effect on calcium excretion. The total 24-hr excretion was markedly increased compared with that found on constant activity but on the same dietary regimen, and 78 percent of the increase occurred between 0900 and 1800 hr.

170. Morse, B. S. Erythrokinetic changes in man associated with bedrest. *Clinical Research* 16:240-254, 1968.

Purpose: To investigate the loss of red cell mass and the accompanying erythrokinetic changes that occur during 35 days of bedrest.

Procedure and methods: Thirteen normal, healthy men (18 to 33 yr) were subjected to a 20-day control period, 35 days of bedrest, and 20 days of recovery. Eight other men (18-40 yr) served as ambulatory controls. All blood samples were obtained at 0730 hr with the subjects in a basal condition. The diet was not rigidly controlled.

Results: At the end of 35 days of bedrest, there was an average loss of 183 ml of red cell mass (range 0 to 328 ml). After 3 weeks of recovery, red cell mass was still significantly below control levels.

During bedrest, plasma volumes decreased 200 ml. At the end of recovery, plasma volumes were elevated above control values. During the first 2 days of bedrest, hematocrit increased from 44 to 47 percent and remained stable during the remainder of bedrest. During recovery, hematocrit decreased rapidly from 45 to 40 percent and slowly increased during the ensuing 3 weeks but never quite returned to control levels. Changes in hemoglobin concentration paralleled those of hematocrit and thus mean corpuscular hemoglobin remained stable.

Conclusions: The loss of red cell mass during bedrest was most likely due to a decreased rate of erythropoiesis.

171. Murray, R. H. and M. McCally (eds.). Hypogravic and Hypodynamic Environments. Proceedings of a Conference at French Lick, Indiana, June 16-18, 1969. NASA SP-269, 1971.

Table of contents:

A. Weightlessness

1. Dietlein, L. F. Spaceflight deconditioning: an overview of manned spaceflight results.
2. Johnson, P. C., C. L. Fischer, and C. Leach. Hematologic implications of hypodynamic states.
3. Mack, P. B. Bone density changes in the astronauts during spaceflight.
4. Whedon, D. G. and L. Lutwak. Metabolic studies of the Gemini 7 14-day orbital spaceflight.
5. Discussion

B. Immobilization

6. Nordin, B. E. C., A. Horsman, and L. Bulusu. Assessment of bone mass in relation to inactivity.
7. Cameron, J. R., J. M. Jurist, and R. B. Mazess. Some physical methods of skeletal elevation.
8. Jowsey, J. Bone at the cellular level: the effects of inactivity.
9. Zollinger, R. M., Jr., and F. D. Moore. Estimation of total skeletal mass in man by radioisotope dilution.
10. Kazarian, L. E. and H. E. von Gierke. Disuse atrophy in *Macaca Mulatta* and its implications for extended spaceflight.
11. Abendschein, W. F. and G. W. Hyatt. Nondestructive measurement of some physical properties of bone.
12. Discussion

C. Cardiovascular effects of bedrest

13. Blomquist, G., J. H. Mitchell, and B. Saltin. Effects of bedrest on the oxygen transport system.
14. Hyatt, K. H. Hemodynamic and body fluid alterations induced by bedrest.
15. Schmid, P. G., M. McCally, T. E. Piemme, and J. A. Shaver. Effects of bedrest on forearm vascular responses to tyramine and norepinephrine.
16. Lancaster, M. C. and J. H. Triebwasser. The effect of total body exercise on the metabolic, hematologic and cardiovascular consequences of prolonged bedrest
17. Discussion

D. Metabolic effects of bedrest

18. Donaldson, C. L., D. E. McMillan, S. B. Hulley, R. S. Hattner, and J. H. Bayers. The effects of long-term bedrest on mineral metabolism.

19. Vogel, J. M. Changes in bone mineral content of the os calcis induced by prolonged bedrest.

20. Lindan, O. The relationship between the diurnal and meal-driven rhythms of kidney functions in subjects at rest.

21. Piemme, T. E. Effects of two weeks of bedrest on carbohydrate metabolism.

22. Lecocq, F. R. The effect of bedrest on glucose regulation in man: studies in progress.

23. Lancaster, M. C. Hematologic aspects of bedrest.

24. Discussion

E. Immersion: deconditioning countermeasures

25. McCally, M. and C. C. Wunder. Immersion techniques and the evaluation of spaceflight deconditioning countermeasures.

26. Graver, O. H. Body fluid regulation during immersion.

27. Webb, P. Deconditioning and its prevention by simulating the hydrostatic gradient.

28. Discussion

F. Research direction

29. Discussion

172. Myasnikov, A. L., R. M. Akhrem-Akhremovich, L. I. Kakurin, Yu. T. Pushkar', N. M. Mukharlyamov, V. S. Georgiyevskiy, Yu. N. Tokarev, Yu. A. Senkevich, B. S. Katkovskiy, A. N. Kalinina, M. A. Cherepakhin, V. A. Chichkin, V. K. Filosofov, and P. G. Shamrov. The effect of a prolonged hypokinesia on the human blood circulation. *Aviatsionnaya i Kosmicheskaya Meditsina (Moscow),* 1963, pp. 368-371.

Purpose: To investigate cardiovascular function during bedrest.

Procedure and methods: Four men (22 to 24 yr) were kept in the horizontal position for 20 days and sat upright in a spacecraft once every 3 to 4 days. Measurements made were pulse rate, arterial pressure, stroke volume, cardiac output, peripheral resistance, isometric contraction, venous flow, and mechanical systole.

Results: During bedrest, pulse rate dropped 14 beats/min; arterial pressure dropped 11 mm Hg; stroke volume was reduced 6 ml; minute volume dropped 1.6 liters; peripheral resistance rose 514 dyne/cm^2/sec; blood flow was reduced in the skin vessels but unchanged in the cephalic vessels. During recovery pulse rate rose from 18 to 34 beats/min; the pulse pressure increase was accompanied by a corresponding rise in minute volume; and peripheral resistance was reduced 238 dyne/cm^2/sec.

173. Nasledov, G. A. and V. N. Filippova. Disturbed motor center co-ordination resulting from immobilization of a limb in man. *Sechenov Physiological Journal of the U.S.S.R.* 44:526-533, 1958.

Authors' conclusions: A definite functional asymmetry in the interaction between the nerve centers for the legs was demonstrated in healthy individuals: on voluntary tensing of the right flexor the left extensor was involuntarily tensed, and on voluntary tensing of the left flexor or the left or right extensor the right flexor was usually tensed involuntarily in each case. Thus, dominance of the center for the right flexor was manifest in the interaction between the motor centers for the legs in man.

Disturbance occurred in the interaction between the motor centers during the time the leg was in plaster, this disturbance being more profound in immobilization of the right leg.

The disturbances in the interaction between centers were made evident by the fact that, when one muscle was voluntarily tensed, all the other muscles examined in both limbs underwent involuntary contraction. Apparently, it is the reciprocal inhibition in the motor apparatus that is primarily affected as a result of the trauma and subsequent immobilization, and excitation spreads widely through the nerve centers, rendering accurate coordination of motor acts difficult. In the case of more prolonged immobilization (20 months), potentials are lacking in all muscles except that voluntarily contracted. This indicates a pathological spread of inhibition in the nerve centers.

In view of the fact that there were no material changes in the strength-duration curve for direct stimulation of the muscles in these patients, the changes observed in the electromyograms must be ascribed to processes occurring in the nerve centers.

174. Oberfield, R. A., F. G. Ebaugh, Jr., E. P. O'Hanlon, and M. Schoaf. Blood volume studies during and after immobilization in human subjects as measured by sodium radiochromate (Chromium-51) technique. *Aerospace Medicine* 29:10-13, 1968.

Authors' abstract: The blood volume of 11 subjects was measured by the use of sodium radiochromate to compare their conditions after long periods of immobilization with those following ambulation. The whole blood volume increased an average of 10.1 percent with a range of −5.3 to 30.9 percent. The red blood cell volume increased an average of 8.6 percent with a range of −6.3 to 22.4 percent. These are statistically significant increases at the 1-percent level. For the plasma volumes, there is a statistically significant increase at the 3.2-percent level if the weights of the subjects before and after immobilization are averaged. However, if the exact height and weight of each subject are used, the plasma volume is not significantly increased at the 5-percent level.

This variation in blood volume is a homeostatic adaptation mechanism not fully elucidated, but it perhaps explains some of the postural changes noted in human subjects after spaceflights or in patients after prolonged bedrest.

175. Olree, H. D., B. Corbin, G. Dugger, and C. Smith. An evaluation of the effects of bedrest, sleep deprivation and discontinuance of training on the physical fitness of highly trained young men. Progress Report, NAS 9-9433, Harding College, Searcy, Arkansas, 1973.

Authors' conclusions: There was a moderate increase in strength variables due to the training in this experiment but the stress which the subjects received caused a negligible change in strength variables. The training program in this experiment resulted in highly significant changes in specific bicycle ergometer variables indicating good increases in cardiopulmonary fitness. Five days of bedrest or 50 hr of sleep deprivation caused comparable drastic decreases in cardiopulmonary fitness. Poststress, the subjects reverted to a normal daily schedule and after 2 weeks they had recovered about half of what they lost. Cardiac output remains relatively constant at a constant workload but stroke volume increases with conditioning and decreases with deconditioning due to stress.

176. Orlova, T. A. Urea content in the blood during prolonged limitation of mobility. *Problemy Kosmicheskoy Biologii* 13:108-109, 1969.

Purpose: To determine the time course of the blood urea content during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs. Urea studies were conducted in four of the subjects from groups IV and V.

Results: On the average, blood urea nitrogen was unchanged after 70 days of bedrest. In shorter studies of 15 to 30 days of restricted movement but not bedrest per se, blood urea nitrogen increased and the maximum increase was observed on the 15th day. In some subjects the urea content decreased to normal levels by the 30th day.

Author's conclusions: These studies indicate that an increase in blood urea content occurs when motor activity is restricted and usually normalizes after prolonged bedrest. This increase in blood urea content appears not to be due to increased nitrogen content of food or to intensified tissue breakdown, but it is most likely due to altered kidney function.

177. Pak, Z. P., G. I. Kozyrevskaya, Yu. S. Koloskova, A. I. Girgor'Yev, Yu. Ye. Bezumova, and Ye. N. Biryukov. Peculiarities of water-mineral metabolism during 120-day hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 7:56-59, 1973.

Purpose: To investigate water and mineral metabolism during bedrest.

Procedure and methods: Four subjects (23 to 44 yr) underwent a 20-day ambulatory control period, then a 120-day bedrest period. Measurements made were plasma volume (Evans blue) urinary-osmolality, sodium, potassium, chloride, and volume; renal plasma flow, glomerular filtration rate, water intake, water balance, body weight, serum-osmolality, sodium, potassium, and chloride.

Results: During the entire bedrest, the subjects exhibited a negative water balance: it was most clearly seen on the 36th, 64th, 83rd, and 96th days. The maximal decrease in body weight was observed on the 83rd day of bedrest. The dynamics of the weight changes corresponded approximately to fluctuations of the water balance: the latter was dependent for the most part on the degree of diuresis because the quantity of fluid drunk was essentially constant.

In the early days of bedrest, there was an increase in urinary volume, the excretion of osmotically active substances including sodium, an increase in the renal plasma flow by 10 to 11 percent and an increase in glomerular filtration rate by 5 percent. These losses were accompanied by a decrease in plasma volume of 11 percent. The changes in water and mineral metabolism varied in cyclic fashion during bedrest.

178. Panferova, N. Ye. Vascular tone in different parts of the body during prolonged restriction of muscular activity. *Kosmicheskaya Biologiya i Meditsina* 6:47-50, 1972.

Author's abstract: During a 120-day bedrest experiment, four test subjects were examined for arterial tone by determining pulse wave propagation and venous tone by the use of occlusion plethysmography and skin-temperature measurements. The above indices recorded for different body areas varied differently. The tone of veins and arteries in the legs, including skin arterioles, increased. The tone of head and hand veins remained unchanged. The tone of head and foot arteries decreased. The tone of large vessels of the elastic type, aorta, carotid artery, and arm artery, did not change. It is probable that variation in vascular tone is one of the mechanisms (supplementing endocrine regulation) responsible for regulating circulating blood volume during hypodynamia.

179. Panferova, N. Ye. and V. A. Tishler. Arterial tone in relation to restricted muscular activity. *Kosmicheskaya Biologiya i Meditsina* 2:56-61, 1968.

Purpose: To investigate the dynamics of some of the indices of arterial tone during chair rest and bedrest.

Authors' abstract: Experimental data are presented concerning the dynamics of some indices characterizing arterial tone prior to, during, and following 5- to 20-day exposure of 16 test subjects to hypodynamia or relative physiological rest (in a chair or bed). Recordings were made of the velocity of the pulse-wave distribution in the aorta and vessels of the arm and leg; calibrated pulse amplitude of the vessels of the second and fourth fingers and toes (mm^3); skin temperature of the chest, forehead, back of the hand and foot, and front part of the shin. Before and after the experiment, the test subjects underwent 15 to 20 min tilt table tests during which time the above indices were recorded. It was found that hypodynamia resulted in an increased constriction of vessels in the lower extremities, including skin arterioles, wheras the tone of the aorta and arm vessels remained virtually unchanged. The constriction of the leg vessels was more pronounced during the post-experiment orthostatic tests in comparison with that observed prior to the experiment. However, the adaptation range of the investigated indices was narrowed due to changes of baseline pretest values.

180. Panferova, N. Ye., V. A. Tishler, and T. G. Popava. Effect of prolonged bedrest on the dynamics of cardiac contractions in man. *Kosmicheskaya Biologiya i Meditsina* 1:75-78, 1967.

Purpose: To investigate the effect of prolonged mobility limitation on cardiac dynamics.

Procedure and methods: Fifteen men were confined to a seat for 20 days with specially selected angles for holding the ankle, knee, hip, and elbow joints in fixed positions. While in this position the subjects performed physical exercises for maintaining muscle tone and preventing joint pain. Fifteen cardiac function tests were run before and after the chair rest.

Results: After 20 days of chair rest, the subjects exhibited an increased pulse rate (+10 percent), increased diastolic pressure (+7.5 percent), decreased systolic pressure (−4.2 percent), decreased pulse pressure (−20 percent), and decreased stroke volume (−18 percent). Pulse wave velocity was constant.

The absolute values of the mechanical and general systole and diastole decreased somewhat, but the absolute value of the electrical systole increased. There was a shortening of the left-ventricular systolic expulsion period and a lengthening of the tension period at the expense of an increase induration of the asynchronous and isometric contraction phases. Thus, during chair rest, the phase structure of the cardiac contraction cycle changed so that the duration of the passive part of systole increased. This fluctuation was reflected in a reduced intrasystolic index and an increased myocardial tension index. Simultaneously, the initial rate of increase of intraventricular pressure decreased as did the mean rate of left-ventricular evacuation.

Authors' conclusions: The myocardial hypodynamia syndrome in athletes and other individuals in the evening hours suggests a predominance of vagus nerve tone, as indicated by a slowing of the pulse rate and an increase in the intensity of the pulse sinus arrhythmia. After chair rest with the limitation of muscular activity, the myocardial hypodynamic syndrome is accompanied by a slight tachycardia, a reduction in pulse arrhythmia, and increased diastolic pressure. These results support the hypothesis that cholinergic effects are not the basic factor responsible for the appearance of this syndrome.

181. Panov, A. G. and V. S. Lobzin. Some neurological problems in space medicine. *Kosmicheskaya Biologiya i Meditsina* 2:59-67, 1968.

Authors' abstract: A simulation experiment was carried out to evaluate disturbances in functioning of the nervous system which may occur during different stages in manned spaceflight. Four healthy male volunteers (age 22) were restricted to a recumbent position for 72 days. An analysis of clinical observations, neurological surveys, and other tests revealed three stages in the development of shifts caused by prolonged bedrest. The last stage, developing after 20 days of bedrest, was of the greatest significance. This stage is characterized by the development of disturbances in the higher nervous system. At this stage one of the test subjects exhibited acute neurotic reactions which made it necessary to stop the experiment. Other test subjects exhibited sleep and emotional disorders. All the test subjects also exhibited muscular atrophy, reduced muscular strength, development of manifestations of oral automatism, and other disorders of the nervous function. Some disturbances were also observed during a tilt-table test and exposure to accelerations. The authors believe that the concept of the phasic development of nervous disorders will allow prophylactic and therapeutic measures to be predetermined. They give recommendations on how to choose sleep-inducing, sedative, anaphylactic, and other drugs and also discuss their peculiar effects during spaceflight.

182. Panov, A. G., V. S. Lobzin, and V. A. Belyankin. Changes in the functions of the nervous and muscular systems under the influence of prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:133-147, 1969.

Purpose: To investigate the neuromuscular system during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' summary: Nervous-system changes were studied in 16 healthy young males under the influence of prolonged (up to 70 days) hypodynamia. Definite staging of the changes were discerned. The initial stage was characterized by early adaptive reactions, and the intermediate stage by atrophy of muscles, especially those of the lower legs. The advent of the third stage (after 20 days of hypodynamia) was marked by disturbances to higher nervous activity: disturbed sleep, emotional disturbances, and other asthenic symptoms. An acute neurotic state in which there was an importunate and uncontrollable desire to move developed in one of the subjects on the 20th day, and he was obliged to leave the experiment. Thereafter, with the asthenic state as background, oral-automatism phenomena and signs of "pyramidal insufficiency" made their appearance among the remaining subjects. The latter were manifested in increased tendon and periosteal reflexes in the right extremities, loss of strength in these extremities, decrease or loss of the abdominal and plantar reflexes, again on the right side, smoothing of the right nasolabial fold, and deviation of the tongue to the right. This set of signs indicated the development of interhemispheric asymmetry with hypodynamia, with functional insufficiency of the dominant hemisphere. This syndrome was noted in 14 of 16 subjects. A gradual recovery of nervous-system functions was observed after reactivation. The authors attach great importance to systematic exercising of the standing and supporting mechanisms, preferential physical exertion on the left extremities, and autogenous conditioning in its psychotonic modification as prophylactic measures against these disturbances.

183. Parin, V. V., T. N. Krupina, G. P. Mikhaylovskiy, and A. Ya. Tizul. Principal changes in the healthy human body after a 120-day bed confinement. *Kosmicheskaya Biologiya i Meditsina* 4:59-64, 1970.

Purpose: To investigate the effect of various drugs for the prevention of 120-day-bedrest deconditioning.

Procedure and methods: Ten men were divided into three groups and following a 20-day control period were put to bed for 120 days, followed by a 30-day recovery period: group 1 (4 men)–no exercise control; group 2 (3 men)–received pituitrin in a dose of 5 oxytocin activity units from the beginning of the experiment, from the 22nd through the 90th day, DOCA at dose of 1 ml every other day; and group 3 (3 men)–received methandrostenolone in a dose of 5 mg/day from the lst through the 28th day and a dose of 10 mg/day from the 72nd to the 100th day.

The subjects were always in the horizontal position. They ate 3 meals/day. Caloric intake in the control and recovery periods was 2919 and 2408 kcal/day during bedrest. Measurements and blood sampling was performed every 10 to 15 days and larger blood collections were made at the end of each month.

Results: Clinical observations revealed that already during the first 2 or 3 days all the subjects complained of pain in different parts of the body, difficulty in falling asleep, headache, desire to get up, etc. By the end of the first week, most of the subjects became calmer; they seemingly adapted to the hypokinetic conditions; pain and unpleasant sensations were reduced. Somewhat later, during the fourth to fifth weeks, changes in the nervous system were more clearly expressed; these involved primarily impairments in the autonomic parts of the nervous system. At this same time there were changes in the behavior of these subjects and impaired sleep (both with respect to falling asleep and the depth of sleep). These symptoms became more clearly expressed with lengthening of the duration of hypokinesia and by the end of the second and beginning of the third month the nervous system changes had taken the form of two distinct syndromes: autonomic-vascular dysfunction and neuropsychic asthenization of the organism. Beginning with the end of the first month, the neuromuscular excitability and bioelectric activity of the muscles revealed a decrease in muscle tone and impaired trophicity manifested in a progressive muscular atrophy, particularly in the muscles of the lower leg. By the end of the investigation their circumference had decreased by 5-6 cm. By the end of the third month, all these changes had seemingly stabilized at a new level, not increasing in their intensity until the end of the investigation.

EEG data indicated that on the first day of hypokinesia there was an increased excitability of the cerebral cortex despite normal reactivity. Beginning with the second and running through the middle of the fourth month (the period of maximum development of autonomic dysfunction and body asthenization), there was a progressive change in excitability and reactivity and a decrease in the functional state of the cortex (rapid fatigue, perversion of reactions, rapid onset of dozing, etc.). At the end of the experiment there was a moderate increase in cerebral excitability despite a decrease in reactivity.

The aural analyzer exhibited an increase in hearing thresholds (in the case of air conduction) to 25 db (primarily at high frequencies), whereas for individuals with symptoms of cochlear neuritis during the background period the hearing thresholds increased to 40 db. However, one subject from the first group developed sudden unilateral deafness on the 11th day of hypokinesia. The nature of the clinical picture

184. Patel, A. N., Z. A. Razzak, and D. K. Dastur. Disuse atrophy of human skeletal muscles. *Archives of Neurology (Paris)* 20:413-421, 1969.

Purpose: To describe the histological changes that occur in skeletal muscle in immobilized man.

Procedure and methods: Fourteen male patients were studied who had been immobilized for periods from 4 to 38 weeks for traumatic fractures, spinal tuberculosis, and one man who was comatose for 7 months. None of the patients had either neuromuscular disorders or any evidence of a generalized disease.

The immobilized muscle (plaster cast) and its nonimmobilized mate were biopsied under local anesthesia and all specimens were preserved in formaldehyde solution for paraffin sectioning; some were preserved frozen for sectioning. The latter were cut to about 30μ, treated with neotetrazolium for detection of succinicdehydrogenase activity. Muscle fiber diameter was measured with stage and eyepiece micrometers.

Authors' summary: Disuse atrophy of human voluntary muscle was studied in 14 cases, 11 with immobilization in plaster or traction after fracture of limb bones, 2 in plaster shells for spinal tuberculosis, and 1 with prolonged coma before death. Biopsy of the corresponding muscle of the opposite normal limb was also obtained in some. Frozen sections stained for SDH activity revealed no significant difference in the activity between the immobilized and normal limb muscles.

Histological atrophy of muscle fibers due to disuse was manifest in the form of small or large groups of atrophied fibers in 5 of the 14 cases. Measurements of fiber diameters in frozen and paraffin sections revealed these differences to be statistically significant. There was no correlation between the duration of immobilization and the degree of atrophy or between the latter and the girth of the immobilized limb. Except for relative increase of muscle nuclei in the atrophied fibers, there was no discernible change in the structure of the extrafusal or intrafusal muscle fibers (spindles seen in two cases), connective tissue, blood vessels, or nerves.

185. Pawlson, L. G., J. B. Field, M. McCally, P. G. Schmid, J. J. Bensy, and T. E. Piemme. Effect of two weeks of bedrest on glucose, insulin and human growth hormone levels in response to glucose and arginine stimulation. Aerospace Medical Association Preprints, 1968, pp. 105-106.

Purpose: To investigate possible causes of the abnormal carbohydrate metabolism during bedrest.

Procedure and methods: Four healthy volunteer students in their early twenties underwent a 1-week ambulatory control period, 2 weeks of bedrest, and a final week of recovery. An oral glucose tolerance test was performed on the 5th day of the control and recovery periods and on the 10th day of bedrest. Periodic blood samples after glucose ingestion were analyzed for glucose, plasma insulin, and plasma growth hormone. The response to arginine infusion (30 gm) was measured on the day following glucose tolerance.

Results: Bedrest resulted in marked changes in glucose, insulin, and human growth hormone in response to the oral glucose load. Resting normal values of all three were unchanged by bedrest. Blood glucose levels during bedrest were significantly elevated above corresponding values during the control period at 60 min and at 120 min after glucose ingestion.

During bedrest, plasma insulin was increased above the control levels at 60, 120, and 180 min after glucose ingestion. The total calculated areas under the insulin and glucose curves during bedrest were significantly elevated over control and recovery data. Insulin/glucose ratios were more than doubled during bedrest as compared with the control period.

The expected secondary rise in growth hormone at 180 min after oral glucose was seen in the control and recovery periods, but was not seen in bedrest.

Infusion of arginine resulted in (a) a small nonsignificant rise in blood glucose during the three periods; (b) an augmentation of insulin levels, with a significant increase during bedrest; and (c) an increase in the insulin to glucose ratios during bedrest.

Conclusions: Bedrest, either because of its necessary attendant inactivity or as a consequence of alteration of hydrostatic forces, results in relative intolerance to a glucose load. Further, the secretion of insulin in response to glucose and arginine stimuli is enhanced. During bedrest, a given increment in insulin is less effective in producing a fall in blood glucose than under ambulatory conditions, either because of interference with peripheral utilization or because of increased interference of some unknown mechanism. Among known physiologic antagonists to insulin action are human growth hormone and cortisol.

Since glucose ingestion and arginine infusion resulted in a decreased growth hormone response during bedrest, increase in activity of growth hormone cannot be responsible for the insulin antagonism. An increase in plasma cortisol levels remains as a possible mechanism for the insulin antagonism.

186. Pekshev, A. P. Hemodynamic changes during prolonged hypokinesia on the basis of the dye-dilution method. *Problemy Kosmicheskoy Biologii* 13:50-57, 1969.

Purpose: To investigate the stroke and minute heart volumes, circulating blood mass, hematocrit, the cardiac index, and blood circulation time during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results: When no prophylactics were taken (group 1) there were distinct increases in stroke volume, heart minute volume, and the central (intrathoracic) blood volume, a slight decrease in plasma volume, an increase in hematocrit, and a lengthening of the total blood circulation time. The protective measures (drugs, physical exercises) tended to reduce the adverse responses listed above during bedrest.

187. Pestov, I. D. and B. F. Asyamolov. Negative pressure on the lower part of the body as a method for preventing shifts associated with change in hydrostatic blood pressure. *Kosmicheskaya Biologiya i Meditsina* 6:59-64, 1972.

Purpose: To evaluate the effect of periodic application of lower body negative pressure on orthostatic stability and water balance during 18-hr and 30-day bedrest periods.

Procedure and methods: Eight men, 19 to 21 yr, participated in four series of 18-hr tests with at least a 2-week interval between experiments: Series I – group 1: immersion in water (34° – 35°C) to the neck level in the sitting position; Series I – group 2: bedrest in the horizontal position; Series I – group 3: seated in a chair; and series I – group 4: water immersion in a sitting position in a bath divided horizontally by a tight partition which made it possible to reduce the compensating counterpressure of the immersion medium on the lower part of the body (similar to group 1 except there was a decrease (by 24 mm Hg) in the external pressure from the waist down). In series I, the measurements made were water intake, renal and extrarenal fluid losses, and lower body negative pressure (70° head-up tilt for 20 min) before and after the 18-hr test period. Mechano- and polycardiographic measurements were also taken.

Series II experiments (see A. D. Voskresenskiy *et al.*, 1972). Each series used three subjects: series II – group A1: hypodynamia in the horizontal position for 30 days and twice daily exposure to LBNP for 6 hr/day at −27 mm Hg; series II – group A2: hypodynamia in the horizontal position for 30 days. From the 26th to 30th day, LBNP for 2.5 hr/day with peak pressures −50 to −55 mm Hg; series II – group B: hypodynamia in an antiorthostatic position (4° head downward) for 30 days. Daily vertical treadmill exercise, twice a day, for 1 hr/day from the 1st through 24th day. From 26th to 30th day, daily treadmill exercise for 1 hr/day plus LBNP for 2.5 hr/day with peak values of 36 to 44 mm Hg.

Results: Series I – the results of orthostatic tolerance and water balance were progressively less severe going from groups 1 through 4. In group 1, the Δ pulse rate was 25 beats/min and the water balance was −1500 ml; in group 4, the Δ pulse rate was −2 beats/min and water balance was −600 ml. In group 1 water intake was greatly inhibited, and in group 4 there was copious fluid intake with a reduced diuresis.

Series II – The LBNP regimen used in group A1 was too difficult. In groups A2 and B, the LBNP sessions improved the subjects' overall condition and their emotional state.

Conclusions: Orthostatic tolerance is improved in proportion to the time spent in the upright position. LBNP during water immersion not only prevented orthostatic disorders, but even somewhat increased orthostatic stability in comparison with control values. Maintenance of the upright position and LBNP increased water consumption.

188. Pestov, I. D., M. I. Tishchenko, B. A. Korolev, B. F. Asyamolov, V. V. Simonenko, and A. Ye. Baykov. An investigation of orthostatic stability after prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:231-250, 1969.

Purpose: To investigate orthostatic tolerance after bedrest and to study the effect of various prophylactic measures.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest.

Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5 7-8, and 9-10. This conditinoning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Orthostasis was measured under two positions: (a) the table was inclined 90° from the horizontal and the test lasted 20 min and (b) the table was inclined 70° from the horizontal and the test lasted 15 min. The subjects sat on a saddle on the tilt table.

During the orthostasis tests, the following measurements were made at 1-min intervals: (a) EKG in the standard precardial leads, (b) phonocardiogram, (c) sphygmograms of the carotid, femoral, and radial arteries, and (d) tachoscillogram of the brachial artery.

Results: The control subjects exhibited the greatest decline in orthostatic tolerance; all four subjects fainted after 70-days of bedrest. The best response was seen in group III, who had the physical exerxises. The use of drugs in group II prevented collapse during orthostatic tests. Recovery to pre-bedrest levels was still incomplete a month after bedrest.

189. Petrovykh, V. A., R. V. Kudrova, M. I. Kuznetsov, P. P. Lobzin, I. G. Popov, I. A. Romanova, Yu. K. Syzrantsev, A. M. Terpilovskiy, Yu. F. Udalov, and N. A. Chelnokova. Nutritional state of human subjects kept for long periods in a horizontal position and subsequently exposed to acceleration. *Problemy Kosmicheskoy Biologii* 7:355-363, 1967.

Purpose: To study the nutritional state of human subjects during bedrest.

Procedure and methods: Three subjects (22 to 24 yr) were confined to bed for 10 days (subject C) or 15 days (subjects A and B). During the control period, the subjects ate a diet consisting of 105 gm protein, 126 gm fat, and 371 gm carbohydrate with a caloric value of 3124 kcal/day. During bedrest the subjects ate a diet consisting of 125 gm protein, 105 gm fat, and 307 gm carbohydrate equalling 2745 kcal/day.

Gastric enzyme activity was estimated from the uropepsin content in the urine. Intestinal function was measured from the urinary excretion of indican. Also measured were blood glucose, total lipids, cholesterol and phospholipids; and urininary total nitrogen, amino acids, urea, ammonia, creatinine, uric acid, vitamins C, B_1 and B_2, 4-pyridoxic acid, N_1-methylnicotinamide, oxygen uptake chloride, phosphate, calcium, pH, and titratible acidity. Water metabolism was also studied.

Results: Bedrest had no influence on urinary uropepsin concentration. There was no change in the indican content in the urine. Urinary total nitrogen excretion increased especially during the first days of bedrest that resulted in a negative nitrogen balance. There was an increase in urinary urea ammonia and uric acid during bedrest. During bedrest there were no significant changes in blood total lipids, cholesterol, lipid phosphorus or glucose; urinary pH and titratible acidity were unchanged. Urinary calcium and phosphorus increased. Voluntary water consumption progressively increased during bedrest.

190. Petukhov, B. N. and Yu. N. Purakhin. Effect of prolonged bedrest on cerebral biopotentials of healthy subjects. *Kosmicheskaya Biologiya i Meditsina* 2:56-61, 1968 (same study as Kakurin, 1968; Georgiyevskiy *et al.*, 1968; Cherepakhin, 1968a; Cherepakhin, 1968b).

Purpose: To investigate the bioelectric activity of the cerebral cortex during 62 days bedrest.

Procedure and methods: Six healthy men (22 to 36 yr) were subjected to bedrest for 62 days. Three subjects had no exercise and three were subjected to an exercise training program of progressively increasing intensity (see Cherapakhin 1968a for details). The subjects were exposed to $+G_X$ acceleration before and after bedrest.

An EEG was recorded each 10 to 13 days between 1000 and 1300 hr from both hemispheres while the subjects were confined to a darkened room. During EEG recording, one stimulus (a sound) was given for 1 msec and 5 sec later a light was switched on and left on for 5 sec. The sound served as a conditioned stimulus and the light as an unconditioned stimulus.

Results: In the control period, all subjects had essentially normal bioelectric activity; a rather regular α-rhythm predominated in almost all leads. As bedrest progressed, there was a shift of cortical rhythm in the direction of the slower frequencies. The normal rhythm was not restored after 3 days of recovery. The responses to the indifferent stimuli increased in variability by the third or fourth day of bedrest and response time decreased by the end of bedrest.

Conclusions: The authors attribute the progressive increase in the intensity of the slow waves primarily to the prolonged restriction of muscular activity. Prolonged confinement in a horizontal position with apparent restriction of afferent impulses result in an impaired functioning of the autonomic nervous system and are a part of the general asthenic syndrome.

191. Petukhov, B. N. and Yu. N. Purakhan. Electric activity of leg muscles during standing after a 120-day bedrest confinement. *Kosmicheskaya Biologiya i Meditsina* 5:64-68, 1971.

Authors' abstract: Changes in the electromyograms (EMG) of 10 healthy subjects were studied following a 120-day-bedrest experiment. The test subjects were classified into three groups: the first, a control group, included four persons; the second and third groups included three men each. The second group of test subjects received pituitrin and DOCA to prevent changes in water and mineral metabolism. The test subjects in the third group were given Nerabol to prevent deviations in protein metabolism. Electromyograms were registered from the tibialis and gastrocnemius muscles of the test subjects as they occupied comfortable and strained positions. The records were made twice before the bedrest experiment and 3 or 4 days and 30 days thereafter. The EMG from the gastrocnemius muscle was registered better during comfortable standing. After the hypokinesia the EMG amplitude exhibited a distinct decrease in the test subjects of the first and third groups and a less marked decrease in the second group of test subjects. This was especially typical of the EMG registered from the gastrocnemius muscle.

192. Plantin, L.-O., S. Ahlinder, F. Norberg, and G. Birke. The distribution of proteins between intra- and extravascular spaces in health and disease. *Acta Medica Scandinavica* 189:309-314, 1971.

Authors' abstract: The extravascular distribution of albumin and immunoglobulin G has been studied with special regard to the effect of prolonged bedrest. The EV/IV ratio of these proteins is very much influenced in the conditions studied. The exact effect of posture could not be obtained in this study, but the results should inspire caution in judging the results of metabolic studies in patients confined to bed in relation to controls. Some errors in retained dose measurements have been pointed out. Although the mechanism is unknown, it has been shown that the EV/IV regulation of proteins has been influenced by external means in severely burned patients.

193. Pometov, Yu. D. and B. S. Katkovskiy. Variations in cardiac output and gas exchange at rest during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 6:39-46, 1972 (see Voskresenskiy *et al.,* 1972 for experimental design).

Authors' abstract: A 30-day-bedrest experiment was carried out during which six healthy male test subjects remained in a horizontal position and nine test subjects were in an antiorthostatic position. Variations in hemodynamics and gas exchange as related to basal metabolism were studied. The subjects who were confined strictly to bed revealed a significant decrease in gas exchange, regardless of whether they were horizontal or antiorthostatic. Subjects who performed physical exercises or underwent electric muscle stimulation exhibited a smaller dropoff of the parameters.

The subjects who were in the antiorthostatic position exhibited an increase in cardiac output on account of the stroke volume as early as the first bedrest day, wheras those who remained horizontal revealed it only on the sixth day of bedrest. At later stages in the experiment, certain difference in changes in the recorded parameters were revealed which were evidently associated with the preventive measures employed (physical exercises, negative pressure applied to the lower body, electric muscle stimulation). Possible mechanisms underlying an increase in the cardiac output and stroke volume during early stages in simulated weightlessness are discussed. It is suggested that similar changes may develop during real spaceflights and that feelings and sensations of cosmonauts during the first hours and days of weightlessness may be accounted for by blood redistribution.

194. Popoff, P. and H. Rick. Influence of bedrest duration on electrolyte metabolism in aged patients with special emphasis on peritrochanteric fractures of the femur and the neck of the femur. *Zentralblatt fur Chirurgie* 28:2181-2183, 1967.

Authors' summary: Twenty-one female patients with peritrochanteric fractures of the femur and the neck of the femur and prolonged bedrest were observed for changes in serum electrolytes (sodium, potassium, calcium, chloride, phosphate) as well as total protein, urea, and electrophoresis. Twelve patients received conservative treatment and eight patients were operated upon. Significant changes in the electolytes caused by the trauma of the accident were not observed. Directed electrolyte substitutions were required only after operative intervention and simultaneous internal ailments. As before, intensive nursing care is a critical factor in the achievement of good results of treatment. Shortening bedrest by performing the operation at the earliest possible time is desirable.

195. Portugalov, V. V., E. I. Ilyina-Kaueva, V. I. Starostin, K. D. Rokhlenko, and Z. F. Savick. Morphological and cytochemical studies of hypokinetic effects. *Aerospace Medicine* 42:1041-1049, 1971.

Purpose: To determine the structural and cytochemical changes in red and mixed skeletal muscles of rats exposed to hypokinesia from 1 to 60 days.

Authors' abstract: The problem of hypokinesia is now of greater importance than 3 or 5 yr ago when space research programs included no extended spaceflights. It seems desirable to again discuss certain aspects of the problem related to morphological and cytochemical findings. Experiments were conducted on 240 mature white male rats, half of which were housed in individual small cages where they were rigidly restrained, while the others were kept in a vivarium and used as controls.

Changes in skeletal muscles were detected as early as the first day of exposure. The results indicate that diminished mobility results in changes in certain cytochemical parameters of skeletal muscles. It was shown that skeletal muscles give evidence that decreased function or inactivity of an organ leads to serious changes in its functional state as well as its histochemical state. The direct effect of hypokinetic conditions on the structure of striated muscles appears to involve first of all local disturbances in muscle blood supply that occur due to the restraint model used. These seem to determine the development of pathological changes observed at early stages of the experiment. Animals which were returned to a normal environment after the 60-day hypokinetic test showed incomplete normalization of muscle structure and metabolism even 20 days later, although by that time they had resumed normal motor activity.

196. Prescott, E. J. and E. C. Wortz. Metabolic costs of upper torso exercises vs. torque maneuvers under gravity reduced conditions. *Aerospace Medicine* 37: 1046-1049, 1966.

Authors' summary: Oxygen consumption was measured in subjects doing exercises and torque maneuvers under 1, 1/4, 1/2, 1/6, and 0 g conditions. The results indicate the following: During torque maneuvers, metabolic rate rises as the force of gravity is reduced. Free upper-torso exercise has no significant effect on metabolic rate as the force of gravity is changed. There is no significant difference between oxygen consumption with the subject at rest at 1 g and at reduced gravity. On the basis of the exercise data, it is tentatively suggested that metabolic work penalties observed in low-traction environments apply to external work only.

197. Purakhin, Yu. N., L. I. Kakurin, V. S. Georgiyevskiy, B. N. Petukhov, and V. M. Mikhaylov. Regulation of vertical posture after flight on the 'Soyuz-6'-'Soyuz-8' ships and 120-day hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 6:47-53, 1972.

Authors' abstract: Control of erect posture was studied before and after the Soyuz-6-Soyuz-8 flights (7 cosmonauts) and a 120-day-bedrest experiment (10 test subjects). The study was performed using stabilographic methods and neurological tests; circulation reactions in cosmonauts were also examined. Coordination disturbances were revealed during flight and bedrest experiments. After the flight and experiment they increased and changes in statics and gait appeared. Stabilographic measurements revealed an increase in the amplitude and frequency (especially in the test subjects) of fluctuations of the general body center of mass. The cosmonauts exhibited an increase in pulse rate and arterial pressure. The test subjects also exhibited a pronounced autonomic reaction. These changes were more distinct in the test subjects after the bedrest experiment.

198. Purakhin, Yu. N. and B. N. Petukhov. Neurological changes in healthy subjects induced by two-month hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 2:51-56, 1968.

Purpose: To evaluate the neurological function of subjects during prolonged bedrest.

Procedure and methods: Six healthy men (22 to 36 yr) were used as subjects and most had engaged in sports. They remained in bed for 62 days and three men were non-exercise controls. The exercise group performed 15-30 min of work in the morning and 1-2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased.

The training was performed utilizing springs and large rubber bands. Bands with resistances of 7.5 to 15 kg were used to exercise the shoulder muscles and bands between 15 and 50 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercises. The average energy cost of the exercises was about 7.3 kcal/min (500 to 1000 kcal/day) with a total working time of 75 to 150 min/day.

The calorie intake was 3000 to 3500 kcal/day.

The study included tests of the nervous system, electroencephalographic recordings, physiological tremor, and fluctuations of the body center of gravity (stabilography).

Results: During the first 2 weeks of the experiment the test subjects exhibited symptoms of asthenic reactions in their behavior and nervous system. Later the symptoms became more serious, acquiring the form of neurological symptoms and an asthenic syndrome (neurasthenia). An analysis of data on the tremor, electroencephalogram, and stabilography also indicated the development of changes in the central nervous system, autonomic nervous system, and orthostatic tolerance in response to long-term hypokinesia. Functional shifts were accompanied by morphological changes in the muscular system.

Conclusions: Physical exercise during bedrest partially hinders the development of nervous-system asthenization.

199. Rogge, J. D. and W. W. Moore, Influence of lower body negative pressure on peripheral venous ADH levels in man. *Journal of Applied Physiology* 25:134-138, 1968.

Authors' abstract: Fluctuations in the blood concentration of antidiuretic hormone (ADH) probably play a role in the diuresis seen during weightlessness and the antidiuresis caused by lower body negative pressure (LBNP). Seven human subjects were exposed to 30-min periods of LBNP at −40, −30, and −20 mm Hg and peripheral venous blood samples were assayed for changes in ADH concentration. The −40 and −30 mm Hg pressures caused significant mean rises ($P < 0.01$) in the blood ADH level, but the −20 mm Hg pressure caused no rise in the mean blood ADH level. When these results are correlated with those from other experiments, they suggest that the ADH rise is due to a shift of blood from the thorax to the lower extremities with subsequent release of intrathoracic baroreceptor inhibition of ADH secretion. Apparently, −20 mm Hg LBNP does not pool a volume sufficient to cause a rise in the ADH level.

200. Rose, G. A. Immobilization osteoporosis. A study of the extent, severity, and treatment with bendrofluazide. *British Journal of Surgery* 53:769-774, 1966.

Purpose: To investigate immobilization osteoporosis.

Author's summary: Urinary-calcium measurements have been made on 75 male and 64 female patients. Full balance studies were carried out on 4 of the young immobilized men. Two of these were studied before and during bendrofluazide therapy. Balance studies were carried out on an additional woman during the recovery period following immobilization.

Hypercalciuria was most marked in young men, who showed markedly raised faecal calcium due to failure to absorb dietary calcium. The women showed little or no rise in urinary calcium. There is no evidence that calcium balances become positive during remobilization.

Bendrofluazide lowered urinary calcium in two cases: one showed no change in faecal calcium, but in the other case there was a matching rise in faecal calcium. Bendrofluazide is recommended for immobilized young men and may have a role in long-distance spaceflights. In long-distance space travel, women may prove less liable than men to develop osteoporosis.

201. Ryabkova, Ye. G. and I. I. Shantyr'. Regional arterial oscillographic indices during hypodynamia. *Problemy Kosmicheskoy Biologii* 13:228-230, 1969.

Purpose: To study the state of the cardiovascular system during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results: Marked changes in arterial pressure and vascular tone were observed. During the first 20 days the maximum (systolic) pressure in the vessels of the arms was unstable, but showed a persistent downward tendency. From the 40th through the 50th day, it rose to original values and then declined again. The maximum pressure in the vessels of the lower legs dropped more sharply and stabilized at this lower level 30 days after the beginning of bedrest.

The minimum (diastolic) pressure in the vessels of the arms and legs did not vary as widely: it decreased in the brachial arteries and rose gradually in the vessels of the lower leg.

During bedrest there was an increase in vascular tone. A distinct drop in arterial pressure and increased vascular tone in the vessels of the legs were observed for several days following $+G_X$ centrifugation. The pressure and tone changes did not return to control levels during 14 days of recovery. In the exercised and occlusion-conditioned subjects, pressure and tone values remained within normal limits.

202. Ryback, R. S. and O. F. Lewis. Effects of prolonged bedrest on EEG sleep patterns in young, healthy volunteers. *Electroencephalography and Clinical Neurophysiology* 31:395-399, 1971.

Purpose: To study EEG sleep patterns during prolonged bedrest.

Authors' summary: The bedrest study involved eight subjects, 18-24 yr of age, and was divided into control, experimental (bedrest, BR), and recovery phases of 5, 5, and 6 weeks, respectively. During the bedrest period, four subjects continued to exercise on the total body ergometer while confined to bed, while the remainder acted as controls (without exercise). All subjects, except for the controls during the bedrest period, performed 600 kcal of exercise a day.

Subjects were paired and recorded together: 1 and 8; 2 and 7; 3 and 6; 4 and 5. This grouping remained the same throughout the study. A total of five recordings were made: one during baseline, two during bedrest (BR_1 and BR_2), and two during recovery. Baseline mean percentages of total night sleep were: rapid eye movement (REM) = 24.64; stages 1 + 2 = 58.95; stages 3 + 4 = 16.44; and stage 4 = 4.62. A Mann-Whitney U test (two-tailed) was performed on all data. A significant increase ($P < 0.01$) in deep sleep (stages 3 + 4) and a decrease ($P < 0.005$) in light sleep (stages 1 + 2) for the entire group (non-exercise, NE, and exercise, E) is seen when the entire BR period is combined (BR_1 + BR_2) and compared to baseline values. There was no significant change in REM, although there was a tendency in the NE group for decreased REM sleep. With recovery (R_1 + R_2), the increase in deep sleep remains but is not significant ($P > 0.05$: <0.1) as is the decrease in light sleep relative to baseline values. However, stage 4 for the entire group showed a significant ($P < 0.05$) increase during bedrest (BR_1 + BR_2) and recovery (R_1 + R_2) relative to baseline values. When E and NE are compared separately during bedrest to baseline values for deep sleep (stages 3 + 4), only the Ne group shows significant differences ($P < 0.05$), although there is a progressive increase in deep sleep for the E groups over the bedrest period. Four to 6 weeks of recovery was necessary to return to pre-bedrest exercise and treadmill performance levels, especially for the no-exercise groups.

203. Ryback, R. S., O. F. Lewis, and C. S. Lessard. Psychobiologic effect of prolonged bedrest (weightless) in young, healthy volunteers (study II). *Aerospace Medicine* 42:529-535, 1971.

Authors' abstract: Sleep data, including EEG recording, psychological testing, and psychomotor performance, were obtained from 8 young, healthy men subjected to prolonged bedrest. The study was divided into control, experimental (bedrest), and recovery phases of 5, 5, and 6 weeks, respectively. During the bedrest period, four subjects continued to exercise while the remainder acted as controls (without exercise). With the onset of bedrest, an increase in deep sleep (stages 3 and 4) and a decrease in light sleep (stages 1 and 2) was observed, especially in the nonexercise group. An additional or ninth subject was recorded while napping during the day and it was shown that napping decreased the amount of time spent in deep sleep that night relative to control nights. Psychological testing revealed an increase in anxiety, hostility, and depression just in anticipation of being put to bed and psychomotor testing demonstrated a decrease in handgrip in the nonexercise group during bedrest. The exercise group improved its handgrip strength during bedrest and recovery.

204. Ryback, R. S., R. W. Trimble, O. F. Lewis, and C. L. Jennings. Psychobiologic effects of prolonged weightlessness (bedrest) in young healthy volunteers. *Aerospace Medicine* 42:408-415, 1971.

Purpose: To study sleep, affect, neurological function, and psychomotor performance during 5 weeks of bedrest.

Procedure and methods: Eight men (18 to 22 yr) underwent a 5-week ambulatory control period, 5 weeks of bedrest, and 6 weeks of recovery. During bedrest four subjects were non-exercise controls and the other four subjects continued to exercise on the total body ergometer and performed 200 kcal of work three times per day. During the entire study all subjects consumed 3334 kcal/day, which consisted of 160 gm protein, 104 gm fat, and 445 gm carbohydrate.

During bedrest sleep, data were recorded utilizing an EEG, affect was studied utilizing various psychological tests, and extensive clinical neurological examination was performed during the control period and at the end of bedrest, and four psychomotor performance tests (Mercury, Rater, Multidimensional Pursuit Task, and Neptune) were given once per week during the control period and once per week during the recovery period.

Results: Both groups of subjects (exercise, 15.83 percent; no exercise, 16-85 percent) spent a larger portion of their sleep time in deep (delta) sleep during the bedrest period than during the control period. There was a tendency for deeper sleep in the no-exercise group. During the recovery period, the amount of deep sleep decreased (11.69 percent) but did not reach control levels (7.2 percent). During bedrest, REM sleep increased and there was a further increase during recovery. The number of subjectively remembered and recorded dreams increased for both groups during bedrest and decreased toward baseline values during the recovery period. Throughout the study and especially during the recovery period, dreams dealt mainly with future plans and expectations. During the control period a few dreams revealed homosexual conflict. As bedrest approached and began, the dreams were concerned more with control, escape, dependence, independence, disruption of the study by the subjects or others, death, and fear of physical degeneration (especially in the no-exercise group). During bedrest many dreams dealt with traveling, riding, or moving and there was an increase in dreams having sexual content. As bedrest ended, many dreams indicated some separation anxiety and the fear that the physical degeneration and loss of strength would persist.

Before bedrest, the exercise group had a significantly higher mean score on the Measurement of Depression (SDS) test compared with the no-exercise group. During bedrest, the entire group had a significantly higher mean on the SDS and on the anxiety, depression, and hostility scales of the Multiple Affect Adjective Check List. During bedrest, the no-exercise group increased markedly on the SDS test while the exercise group remained essentially the same as during the control period. During the recovery period, a comparison of the exercise and no-exercise groups showed a significantly higher mean for the no-exercise group on the anxiety and depression scales of the MAACL and an even greater increase in the SDS: there was no difference between groups on the hostility scale. On the Rorschach test the no-exercise group tended to give more "pathological" type of responses.

There were no differences between groups in the pre-post-bedrest scores on the psychomotor performance tests, but on all subjects there was a significant decrement only on both (reaction time and hand steadiness) Mercury tests.

After bedrest there was a marked decrease in treadmill endurance that, in the no-exercise group, did not return to control levels until the beginning of the fifth week of recovery.

Conclusions: Prolonged bedrest may be understood as a more subtle form of sensory deprivation. It appears that this deprivation is not just environmental as related to the five senses, but a general decreased input neurologically from the muscular system *per se*.

The non-exercise group had more severe symptoms than the exercise group. Prolonged bedrest results in considerable psychological as well as physiological stress. It may "be better to burn out, than to rust out."

205. Saiki, H., M. Nakaya, and C. Sekiguchi. Characteristics of sleep under simulated weightlessness. *Aerospace Medical Association Preprints,* 1971, pp. 62-63.

Purpose: To compare the difference of electroencephalographical and electrooculographical sleep patterns with other physiological functions of human subjects between water immersion and bedrest in daytime and nighttime.

Procedure and methods: Experiments of 1-night duration – Two human subjects after a normal daytime life were fixed in a supine bedrest position for 4 hr. After this preconditioning, the subjects were immersed in water to their neck levels for 8 hr of nighttime sleep. During water immersion period, the lights were off, the environment was kept quiet, and the water at 33°-35°C. Two channels of EEG, from the frontal and the parietal parts of the head, and signals of awakening were recorded continuously. Rectal temperature was recorded continuously. Urine volumes and contents of ascorbic acid, creatine, K, Na, and catecholamine were measured.

Experiment of 3-day duration – One subject was placed in 3-day bedrest and 3-day water immersion. After awakening in the morning, he was allowed to get up only 30 min for excretion of feces and body weighing, etc. The same experiments as in the short time duration were performed continuously. In addition, EOG from the outer corner (canthus) of one eye and ECG were continuously recorded.

Results: The characteristics of the electroencephalographic sleep pattern of water immersion period can be summarized as follows: (1) shortening of total length of sleep period, (2) interruption of total sleep period by many and long wakefulness periods, and (3) general shortening of the deep-sleep stage. Such characteristics were also found in the bedrest sleep period, but they were clearly more remarkable in the water immersion period.

On the bedrest sleep, during the 3-day bedrest life, the characteristics mentioned above appeared more clearly in the sequential appearance of sleep stages for a subject on three successive nights of sleep than in 1-night experiments. In the 3-day experiment, eye movement was recorded and paradoxical sleep stage patterns were checked. In the second and third nights' sleep in bedrest, fairly regular periodicity and almost "normal" sleep patterns were revealed.

Urine volume, potassium, and sodium excretion decreased by the day in water immersion. Calcium excretion increased by the day. This was not observed in the bedrest except the case of urinary volume.

Conclusions: By short-time water immersion, the sleep patterns were changed. It is characterized by shortening of the duration of sleep and shallowing of the depth of sleep.

By 3 days successive water immersion, general cycles of the sleep patterns were changed remarkably: (1) stage 0 (awake) is more frequent, (2) stage 1-REM (paradoxical sleep) and stage 4 (deepest stage) were shortened, and (3) in the case of bedrest, stage 1-REM is distributed at the end of the sleep and stage 4 is distributed mainly at the beginning of the sleep. And in the case of water immersion, stage 1 is concentrated more at the beginning of the sleep and stage 1-REM is removed to the middle of the sleep. The shortening of the REM stage and stage 4 is thought to influence detrimentally the body if they are continued for a long duration. Data obtained on cardiovascular functions, urine excretion, water, mineral, vitamin, hormonal metabolism, and energy utilization by muscular activity were not revealing of any explanation of the changes in the sleep pattern.

206. Saltin, B., G. Blomqvist, J. H. Mitchell, R. L. Johnson, Jr., K. Wildenthal, and C. B. Chapman. Response to exercise after bedrest and after training. A longitudinal study of adaptive changes in oxygen transport and body composition. *Circulation* (Supplement) 7:38:VII-1 to VII-78, 1968.

Purpose: To investigate the effects of bedrest and physical training on submaximal and maximal work performance.

Authors' summary: The effects of a 20-day period of bedrest followed by a 55-day period of physical training were studied in five male subjects, aged 19 to 21. Three of the subjects had previously been sedentary, and two of them had been physically active. The studies after bedrest and after physical training were both compared with the initial control studies.

Effects of bed rest: All five subjects responded quite similarly to the bedrest period. The total body weight remained constant; however, lean body mass, total body water, intracellular fluid volume, red cell mass, and plasma volume tended to decrease. Electron microscopic studies of quadriceps muscle biopsies showed no significant changes. There was no effect on total lung capacity, forced vital capacity, 1-sec expiratory volume, alveolar-arterial oxygen tension difference, or membrane diffusing capacity for carbon monoxide. Total diffusing capacity and pulmonary capillary blood volume were slightly lower after bedrest. These changes were related to changes in pulmonary blood flow. Resting total heart volume decreased from 860 to 770 ml.

The maximal oxygen uptake fell from 3.3 in the control study to 2.4 liter/min after bedrest. Cardiac output, stroke volume, and arterial pressure at rest in supine and sitting positions did not change significantly. The cardiac output during supine exercise at 600 kpm/min decreased from 14.4 to 12.4 liter/min, and stroke volume fell from 116 to 88 ml. Heart rate increased from 129 to 154 beats/min. There was no change in arterial pressure. Cardiac output during upright exercise at submaximal loads decreased approximately 15 percent and stroke volume 30 percent. Calculated heart rate at an oxygen uptake of 2 liter/min increased from 145 to 180 beats/min. Mean arterial pressures were 10 to 20 mm Hg lower, but there was no change in total peripheral resistance. The A-V O_2 difference was higher for any given level of oxygen uptake. Cardiac output during maximal work fell from 20.0 to 14.8 liter/min and stroke volume from 104 to 74 ml. Total peripheral resistance and A-V O_2 difference did not change. The Frank lead electrocardiogram showed reduced T-wave amplitude at rest and during submaximal exercise in both supine and upright position but no change during maximal work.

The fall in maximal oxygen uptake was due to a reduction of stroke volume and cardiac output. The decrease cannot exclusively be attributed to an impairment of venous return during upright exercise. Stroke volume and cardiac output were reduced also during supine exercise. A direct effect on myocardial function therefore cannot be excluded.

Effects of physical training: In all five subjects, physical training had no effect on lung volumes, timed vitalometry, and membrane-diffusing capacity as compared with control values obtained before bedrest. Pulmonary capillary blood volume and total diffusing capacity were increased proportional to the increase in blood flow. Alveolar-arterial oxygen tension differences during exercise were smaller after training, suggesting an improved distribution of pulmonary blood flow with respect to ventilation. Red cell mass increased in the previously sedentary subjects from 1.93 to 2.05 liter, and the two active subjects showed no change.

Maximal oxygen uptake increased from a control value of 2.52 obtained before bedrest to 3.41 liter/min after physical training in the three previously sedentary (+ 33 percent) and from 4.48 to 4.65 liter/min in the two previously active subjects (+4 percent). Cardiac output and oxygen uptake during submaximal work did not change, but the heart rate was lower and the stroke volume higher for any given oxygen uptake after training in the sedentary group.

In the sedentary subjects, cardiac output during maximal work increased from 17.2 liter/min in the control study before bedrest to 20.0 liter/min after training (+16.5 percent). Arteriovenous oxygen difference increased from 14.6 to 17.0 ml/100 ml (+16.5 percent). Maximal heart rate remained constant and stroke volume increased from 90 to 105 (+17 percent). Resting total heart volumes were 740 ml in the control study before bedrest and 812 ml after training.

In the previously active subjects, changes in heart volume, maximal cardiac output, stroke volume, and arteriovenous oxygen differences were less marked.

Previous studies have shown increases of only 10 to 15 percent in the maximal oxygen uptake of young sedentary male subjects after training. The greater increase of 33 percent in maximal oxygen uptake in the present study was due equally to an increase in stroke volume and arteriovenous oxygen difference. These more marked changes may be attributed to a low initial level of maximal oxygen uptake and to an extremely strenuous and closely supervised training program.

207. Sandler, H., J. E. Greenleaf, B. D. Newsom, and S. Rositano. Lower-body negative pressure (LBNP) as a predictor for $+G_Z$ tolerance after bed rest (BR). Aerospace Medical Association Preprints, 1974, pp. 171-172.

Purpose: To determine whether lower-body negative pressure (LBNP) served as a predictor for observed $+G_Z$ tolerance.

Procedure and methods: Fifteen male subjects, ages 19-24 yr, were studied as two groups before and after 14 days of complete bedrest. In the first group of seven subjects, tolerance time and changes in heart rate and blood pressure were determined during 5-min incremental steps of −20 −30 and −40 mm Hg LBNP and compared with similar responses to randomly presented profiles of $+2G_Z$ (11 min), $+3G_Z$ (3-1/2 min), and $+4G_Z$ (3 min). In the remaining eight subjects (second group, studied 1 yr later, not same subjects), identical variables were measured during 15-min continuous exposure to −50 mm Hg LBNP and compared to findings (duplicate exposures) until greyout or blackout at $+2.5G_Z$ and $+3G_Z$. A gradual ramp to peak G (0.03G/sec) was used in both studies. Heart rate was measured by sternal leads, blood pressure by automated cuff and microphone at 1-2-min intervals during all procedures. Control values represented averages for measured parameters for the 5-min period immediately preceding LBNP or acceleration exposure.

Results: Time duration of LBNP had poor correlation with acceleration tolerance. All subjects were able to complete the 15-min LBNP test procedures prior to bedrest. Nine subjects had significant degradations in acceleration tolerance times after bedrest and five additional subjects with similar decreases at a 50 percent level were all able to tolerate the entire LBNP regimen after bedrest. Only one subject in the first group had a decreased tolerance time to LBNP after bedrest, terminated due to syncope. Blood pressure response which differed during the two tests were not compared. Magnitude of LBNP heart-rate changes from control values failed to correlate or improve predictive indices with decreased acceleration time. Average decrease in tolerance time for group one subjects was 30 percent at $+2G_Z$, 32 percent at $3G_Z$, and 27 percent at $+4G_Z$. Similar decreases for group two subjects were 73 percent at $+2.5G_Z$ (average control value 10.5 min) and 87 percent at $+3G_Z$ (average control value 8.6 min).

Conclusions: It is concluded from these studies that LBNP serves as a good provocative test for cardiovascular response to $+1G_Z$ before and after bedrest, but does not serve as a quantitative predictor for acceleration tolerance under these conditions. It appears from these findings that these procedures measure different responses. LBNP measures response to graded, controlled decreases in venous return where blood is pooled in the abdomen and/or legs. Response to +G involves response to a similar decreased venous return of a much larger magnitude, physical impedance to arterial outflow to the head and neck vessels, and stretch of central and peripheral vascular structures.

208. Schmid, P. G., J. A. Shavwr, M. McCally, J. J. Bensy, L. G. Pawlson, and T. E. Piemme. Effects of two weeks of bedrest on forearm venous responses to norepinephrine and tyramine. Aerospace Medical Association Preprints, 1968, p. 104.

Purpose: To determine whether reduced orthostatic tolerance following bedrest is due to alteration in sympathetic nervous system function or to a depression of the responsiveness of vascular smooth muscle to nervous stimuli.

Procedure and methods: Forearm venous responses to tyramine and to norepinephrine were measured in four healthy male subjects during a control session after 8 days of vigorous activity, during a test session after 12 days of bedrest, and during a recovery session 6 days after resuming normal activity.

Venous tone was calculated from measurements of forearm venous volume at a distending venous pressure of 30 mm Hg during brachial artery infusions of tyramine (9.0, 18.0, and 36.0 μg/min) and norepinephrine (0.0375, 0.075, and 0.15 μg/min). Concentrations of norepinephrine and epinephrine in 24-hr collections of urine were obtained for the last 3 days of each session.

Heart rate, systolic, diastolic mean arterial blood pressure changes, and lower limb girth changes were measured before and during an 80° upright tilt on the final day of each session.

Results: Baseline mean arterial blood pressure, heart rate, or venous tone were not different during the control, bedrest, or recovery sessions.

During brachial artery infusions of either tyramine or norepinephrine, heart rate was unchanged during the three sessions whereas venous tone increased significantly in response to both drugs. After bedrest, tyramine produced increases in venous tone which were significantly less than corresponding changes in the recovery session. About four times more tyramine was required after bedrest than after recovery to produce a given response of venous tone. Norepinephrine produced increases in venous tone which were not different in the three sessions.

The quantities of norepinephrine, epinephrine, and total catecholamine in the 24-hr urinary samples for the last 3 days of bedrest were significantly lower than in the control and recovery sessions.

Symptoms of presyncope developed in three of four subjects tested after bedrest; tilting was well tolerated by all subjects after the control and recovery periods. After bedrest, tilt resulted in larger initial increases and larger rates of increase in the girth of the lower leg.

Conclusions: Since venous responses to norepinephrine was not different in the three sessions, it appears that bedrest did not affect the responsiveness of vascular smooth muscle to constrictor stimulation. The attenuation of venous response to tyramine after bedrest suggests that endogenous stores of norepinephrine, which can be released by tyramine and which participate in reflex sympathetic vasomotor adjustments, appear to be depleted after 12 days of bedrest. These results suggest that a decrease in venous vascular responsiveness due to depletion of endogenous norepinephrine may contribute to the orthostatic intolerance produced by bedrest.

209. Schønheyder, F. and P. J. Christensen. The mechanism of creatinuria during immobilization in bed. *Scandinavian Journal of Clinical and Laboratory Investigation* 9:107-108, 1957.

Purpose: To determine if the excess creatine found in the urine of immobilized subjects is due to a surplus of creatine leaving the muscle cell or to a decrease in the uptake of creatinine by the muscle cells.

Results: The results of administration of N^{15}-glycine to one bedrested subject show that the incorporation of N^{15} into creatine (formed in the liver) was far greater than in creatinine during the first days after administration. The results suggest that the increased creatine in blood and urine is caused by a diminished uptake of creatine by the muscles of the endogenously produced creatine. If the reason for the increased creatine was due to greater release from the muscle cell, then there would have been a greater fraction of the N^{15} bound to creatinine because creatinine is formed from creatine in muscle cells. Hence, the N^{15}-labeled creatine never entered the cells. A less likely explanation is that the N^{15} creatine entered and left the muscle cells unchanged.

210. Seregin, M. S., I. G. Popov, Z. N. Lebedeva, O. A. Goryacheva, S. A. Kamforina, P. V. Oblapenko, P. F. Vokhmyanin, and L. A. Andreyeva. Nutrition and metabolism during prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:79-93, 1969.

Purpose: To investigate various nutritional and metabolic parameters during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day.

These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' conclusions: Energy requirement declines, to the accompaniment of a loss of body weight. The level of protein metabolism decreases and a negative nitrogen balance is established; the protein losses averaged 8 gm/day/subject. Calcium excretion increases by 40 percent. Total water losses decrease (by 400-500 gm/day), along with water intake (by 500-700 gm/day), with establishment of water metabolism at a lower balance level; however, the dehydration process that develops at the beginning of hypodynamia is not accompanied by the phenomenon of water deficit. The excretion of vitamins C_1, B_1, B_2, and PP with the urine decreases. The concentration of corticosteroids in the blood and the amounts excreted with the urine decrease. The orthostatic test is accompanied by a significant increase in the function of the hypophyseal-adrenal system. Neither physical exercises nor medication prevented the metabolic disturbances.

211. Simonenko, V. V. Hemodynamic changes during prolonged hypokinesia according to mechanocardiographic data. *Problemy Kosmicheskoy Biologii* 13:42-49, 1969.

Purpose: To investigate the hemodynamics and vascular tone in subjects during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, [illegible]) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjecrs A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Author's conclusions: A predominant influence of the sympathetic innervation on the cardiovascular system is observed during prolonged hypokinesia. Prolonged hypokinesia changes the reaction of a man to cold; this is manifest in phasing of the reactions, weaker responses, and a decrease in the tonicity coefficient of the vessels. The cuff test can serve as a tentative indicator of the compensatory capacity of the cardiovascular system during hypokinesia when a certain amount of blood is excluded from circulation. Physical conditioning mitigates the deconditioning effect of hypokinesia on the cardiovascular system to some degree, but does not prevent it [illegible]

212. Skrypnik, V. G. Changes in the biochemical peculiarities of walking under the influence of hypodynamia according to ichnographic data. *Problemy Kosmicheskoy Biologii* 13:162-170, 1969.

Purpose: To study walking dynamics of subjects undergoing prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results: The initial state of the subjects is characterized by stability of the walking stereotype with the eyes either closed or open and by constancy of the proportions between the component elements of the double step. Eyes-closed walking tends to shorten all length characteristics of the step, but does not affect the proportions between them. After the experiment, all subjects showed disturbance of the habitual walking stereotype, with the eyes both open and closed.

The basic features of the changes from the initial walking background were as follows: (a) a decrease from the initial level in the double-, single-, and half-steps; (b) change in the proportions between the component elements of the double step; (c) reduced ability to walk a straight line; and (d) development of a shuffle.

During the experiment, the series V subjects developed a stronger new walking stereotype than did those of series IV. Immediately after termination of the experiment, the initial walking stereotype was disturbed to a greater degree in the series IV subjects, who had exercised on the bicycle ergometer, than in those of series V, who had exercised on the treadmill.

The process of recovering the initial length dimensions of the double-step elements and their proportional relationships advanced more rapidly in series IV than in V, and was complete a month after the experiment.

In eyes-open walking after the experiment, shortening of the half-steps, forward in series IV and backward in series V, predominates in both groups against a general background of shorter step lengths. The nonuniformity and asymmetry in the shortening of the half-steps after the experiment was probably due to inadequacies of the exercising technique.

To reduce the effect of hypokinesia on walking, it is advisable to increase the vertical component of proprioceptive afferentation for the entire supporting-motor apparatus, and to use exercising machines to impose loads on the gluteal, gastrocnemial, and perineal muscle groups. Long-term use of regular monotonous movements that simulate walking during the 70-day confinement to bed resulted in reconstruction of the original walking stereotype after the experiment. The strength of the walking stereotype reconstructed during confinement to bed depends directly on the exercise facilities used, but was greater in series V than in IV.

Author's summary: Use of the treadmill and bicycle ergometer as physical-conditioning aids for those subject to long-term hypodynamia has various effects on the changes in the habitual walking stereotype and its "recovery." During the first few days after termination of the experiment, the series V subjects were better able to walk unassisted than were those of series IV. To preserve a gait closely similar to the initial level, it is necessary to combine both conditioning procedures. To eliminate hypotonia of the postural, gluteal, gastrocnemial, and perineal muscles, it is necessary to redesign the exercises performed by the subjects and create conditions that impose the greatest load possible on these muscle groups.

213. Sorokin, P. A., A. M. Genin, M. I. Tishchenko, P. V. Vasil'yev, R. I. Gismatulin, and I. D. Pestov. Organizational and methodological principles for the conduct of prolonged hypodynamia researches. *Prolonged Limitation of Mobility and Its Influence on the Human Organism*, edited by A. M. Genin and P. A. Sorokin. Moscow: Nauka Press, 1969, pp. 17-23.

Purpose: To describe the organization and methods for conducting a 70-day bedrest study in 1966 in Russia.

Procedures and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of air-cuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

The measurements made during this investigation were: orthostatic tolerance, transverse ($+G_X$) acceleration tolerance, cardiac output (acetylene method), EKG, venous pressure, thromboelastography, vision tests, nitrogen balance, calcium balance, EEG, basal metabolism, and blood volume.

Comments: Toward the end of bedrest all the subjects showed increased irritability with most of the test procedures that produced unpleasant sensations. In all groups the investigators observed a phenomenon referred to as "migration of authority" where the liveliest, most cheerful, and mobile personality among the subjects of each group acquires "seniority" at the beginning of bedrest. About the middle of the bedrest period, the intragroup hierarchy is readjusted with this subject turning up at the bottom of the ladder. The seniority is then transferred to the quietest, best-balanced subject, and he retains it to the end of the experiment. This indicates an effort on the part of the subjects to provide a stereotype in which external irritants are minimized.

The bedrest period was terminated early for subject K-s because of psychoneurological reactions, for subjects A-v and L-i for appendectomies, and the final acceleration tests for subjects V. M-k, K-ya, and L-i.

214. Sorokin, P. A., V. V. Simonenko, and B. A. Korolev. Clinical observations in prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:24-34, 1969.

Purpose: To analyze the clinical observations from the 70-day bedrest study.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' conclusions: The clinical observations established that prolonged hypodynamia has a definite psychological effect on the subjects.

Freedom to engage in physical activity is a natural need of a healthy human. Its suppression during confinement to bed gives rise to corresponding associations and a desire for exercise that steadily increases in intensity. This would apparently explain the appearance of a kind of "expectation neurosis" in some of the subjects toward the end of the experiments. However, will power and the desire to complete the assigned task prevented the development of neurotic states in most of the subjects. This is indicated by the fact that 15 of the 16 subjects stayed on to finish the job. Only one subject (K-s) was dropped from the experiment because of pronounced psychoneurotic reactions that had developed.

The human suffers unfavorable effects from reduced muscular activity, which is a physiological result of homeostasis and the functions of the cardiovascular, digestive, and other systems of the organism. Our clinical observations indicate a pronounced functional disturbance of the gastrointestinal tract. Unfortunately, we cannot state the nature of these changes with confidence since we were unable to carry out specific investigations in this direction.

The decline in the organism's immunobiological resistance during hypdynamia merits serious attention. Observations made on the subjects showed increased susceptibility and conditionally pathogenic flora. This is indicated by exacerbation of latent foci of infection and the appearance of pyodermias and inflammatory disorders of the upper respiratory passages and otorhinolaryngological organs. There is reason to assume that extremely threatening complications may also be expected to arise in prolonged hypodynamia. This is indicated by the two cases of phlegmonous appendicitis. Vagueness of the clinical picture must be regarded as a peculiarity of the destructive (phlegmonous) appendicitides.

All of the disturbances observed in the subjects can be classified conditionally as postural discomfort effects, temporary functional disturbances, and illnesses. In the first two cases, either no particular intervention by the physician was required or it was limited to advice and the prescription of certain symptomatic medications (analgesics for headache and joint pains, laxatives for constipation, etc.).

The appearance of such disorders as pyodermias, catarrh of the upper respiratory passages, otitis, and urethritis urgently required specific treatment. As a rule, the course of the disorder was sluggish. Appropriate treatment was required after determining the nature of the agent and its sensitivity to antibiotics. Such therapy was usually successful. However, K-ya's case of acute otitis did not respond well to sulfanilimides and antibiotics. Improvement began when the patient was allowed to resume normal motor activity. Finally, special attention must be given to acute appendicitis, a common affliction with potentially grave complications. It is not difficult to diagnose, but in the absence of medical observation, it may not be recognized in time owing to the vagueness of the clinical picture. Timely appendectomies give good results, as is indicated by the favorable outcome of surgical intervention in our subjects.

215. Spealman, C. R., E. W. Bixby, J. L. Wiley, and M. Newton. Influence of hemorrhage, albumin infusion, bedrest, and exposure to cold on performance in the heat. *Journal of Applied Physiology* 1:242-253, 1948.

Authors' summary: The ability of four young men to perform in the heat (33°C, D.B., 28°-29°C., W.B.) certain simple physical tasks (active and passive standing, pedalling a bicycle ergometer) was tested following short (24-hr) periods of bedrest, venesection of 500 cc, exposure to cold (20°C, C.B., 18°C, W.B.) and in control experiments. In all cases, subjects remained in the controlled temperature room for 24 hr prior to testing. The subjects were partially but incompletely acclimatized to the testing temperature by the summer weather and by the short periods of exposure to the higher temperatures of the room. In somewhat similar experiments, the effects of infusing serum albumin and of hemorrhage on performance ability in the heat were studied using four other men as subjects.

Removal of 500 cc of blood (venesection) resulted in an immediate and marked decrease in ability to carry out physical activities (active and passive standing, exercising on bicycle ergometer) in the heat. Several days elapsed before control level of performance was attained again. Performance was affected adversely, but to a lesser degree, following removal of 200 cc of blood. Subjects also performed poorly following confinement to bed and exposure to cold. Infusion of serum albumin in quantity equivalent to 500 cc of blood plasma improved performance.

These various procedures also altered the level of hemoglobin concentration (increase in concentration following experiments on bedrest and exposure to cold; decrease following venesection and albumin infusion) and blood volume. Performance in these experiments correlates well with estimated levels of blood volume, but there is no consistent relationship between performance and hemoglobin concentration.

216. Speckmann, E. W., K. J. Smith, K. M. Offner, and J. L. Day. Physiological status of man subjected to prolonged confinement. AMRL-TR-65-141, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, Dec. 1965.

Authors' abstract: To determine if confinement of men resulted in physiological changes, 12 men in groups of 4 each were confined for 28 consecutive days. During this time, daily measurements of ECG, EEG, blood pressure, respiration, and oral temperature were made. Oxygen consumption and carbon dioxide production were measured daily on 4 subjects for 6 days before and for 6 days following confinement as well as three times weekly during confinement. With 8 subjects, the same measurements were made before, during, and following exercise on a bicycle ergometer at a rate causing the subject to expend an average of 70 additional kcal/hr above resting values. The same metabolic measurements were made on four subjects 2.5 hr postprandial. The metabolic responses to confinement as well as exercise during confinement were measured. In general, there were no significant measured physiological changes from pretest control values resulting from prolonged confinement. Heart rate increased during the first few days and during the last few days of confinement. Although the subjects demonstrated an increased exercise tolerance, they showed a decrease in metabolic efficiency as a result of confinement and/or reduced activity. Resting energy production increased from 93 kcal/hr before confinement to 112 kcal/hr following confinement. A basal energy expenditure of 72 kcal was increased 8 percent due to specific dynamic action. These results suggest that men can readily adjust physiologically to prolonged periods of restricted activity provided sufficient exercise is available to maintain metabolic efficiency.

217. Stepantsov, V. I., M. A. Tikhonov, and A. V. Yermin. Physical training as a method for preventing the hypodynamic syndrome. *Kosmicheskaya Biologiya i Meditsina* 6:64-68, 1972.

Purpose: To evaluate the effectiveness of a vertical treadmill to provide for isotonic exercise with the subject in the horizontal position for 30 days.

Procedure and methods: Three men were confined to bed for 30 days. They exercised for two 1-hr periods daily on a vertical treadmill while they remained in the horizontal position and were supported by a suspension system. The exercise program was designed for maintaining and developing muscular strength, speed of movements, strength and static endurance of different muscle groups, overall body endurance, training the coordination of movements especially when walking and running, and creating an inertial shock load along the longitudinal axis of the body as a means of preventing orthostatic disorders.

The training exercises were organized in a 4-day cycle: Day 1 – maintaining speed and strength; work intensity 1500 kg-m/min or more and energy cost 320 to 360 kcal. Day 2 – maintaining strength and endurance; workload 800 to 1000 kg-m/min, energy cost,380 to 420 kcal. Day 3 – maintaining overall body endurance; workload 500 to 600 kg-m/min, energy cost 45 to 500 kcal. Day 4 – rest; energy cost 100 kcal and performance of submaximal test. Submaximal oxygen uptake was measured every fourth day during bedrest to determine any deleterious effects of bedrest.

Results: From a biomechanical evaluation, the changes of ordinary movements such as walking and jumping were minimal in the exercise group and somewhat greater in the no-exercise control group.

After 30 days of bedrest, both exercise and no-exercise subjects exhibited a decrease in the length of their pace, an increase in transverse deviations from the line of movement, an insignificant increase in the walking rate, and a slight decrease in the vertical displacement of the joints and angles of flexion in the knee and talocalcaneal joints that fell within the range of individual variation. The kinematic changes were somewhat greater in the no-exercise group.

Submaximal oxygen uptake was essentially constant in the exercise group over the bedrest period. The authors assumed the constant oxygen uptake indicated that the exercise program ameliorated the bedrest deconditioning. Oxygen consumption during the 2.5-hr exercise routine under terrestrial conditions averaged

1.0 liter/min while, for the same subject in a horizontal position with a force of 50 kg holding him against the treadmill, the oxygen uptake for the same level of work was 0.8 liter/min.

218. Stevens, P. M. and T. N. Lynch. Effects of 9-alphafluorohydrocortisone on dehydration due to prolonged bedrest. *Aerospace Medicine* 36:1151-1156, 1965.

Authors' abstract: The effects of 9-alphafluorohydrocortisone on the metabolic changes which occur during 6 days of bedrest were studied in four healthy subjects.

During the first 24-hr of bedrest a loss of weight and an increase in urinary water and sodium excretion was noted in all subjects. By the end of the sixth day of bedrest, the hematocrit had increased while the plasma volume had decreased by a mean of 560 cc. The experimental protocol was then repeated but 9-alphafluorohydrocortisone, 2 mg/day, was given during the last two days of bedrest. During this time, the weight increased, water and sodium retention occurred, the hematocrit decreased, and the plasma volume showed a significant increase of 239 cc by the end of the sixth day of bedrest.

It is suggested that part of the "orthostatic deconditioning" described following prolonged bedrest is due to plasma volume loss and that treatment with 2 days of 9-alphafluorohydrocortisone is a simple and efficient way to replete plasma volume losses due to prolonged bedrest.

219. Stevens, P. M., T. N. Lynch, R. L. Johnson, and L. E. Lamb. Effects of 9-alphafluorohydrocortisone and venous occlusive cuffs on orthostatic deconditioning of prolonged bedrest. *Aerospace Medicine* 37:1049-1056, 1966.

Authors' abstract: The effects of 9-alphaflurohydrocortisone and venous occlusive cuffs on the plasma volume and orthostatic tolerance were evaluated following 28 to 78 days of bedrest. In five subjects, the plasma volume and orthostatic tolerance were decreased after 29 days of bedrest, and no further change occurred up to 50 days. Venous occlusive cuffs inflated around the upper thighs of four subjects for 16 hr/day during the last 2 days of a 30-day period of bedrest restored plasma volume but had no significant effect on orthostatic tolerance.

Oral administration of 9-FF 2 mg/day for 2 to 4 days following either 43, 53, or 74 days of bedrest caused complete repletion of plasma volume, but orthostatic intolerance persisted.

220. Stevens, P. M., P. B. Miller, C. A. Gilbert, T. N. Lynch, R. L. Johnson, and L. E. Lamb. Influence of long-term lower body negative pressure on the circulatory function of man during prolonged bedrest. *Aerospace Medicine* 37:357-367, 1966.

Author's abstract: Exposure to lower body negative pressure for 8 hr/day during a 4-week period of absolute bedrest has been shown to significantly maintain orthostatic intolerance and plasma volume. A mean plasma volume loss of 332 cc was seen in the control subjects who were at pure bedrest while test subjects exposed daily to LBNP during bedrest showed no significant change from baseline. Following bedrest, resting recumbent heart rates were significantly higher in control subjects but unchanged in the test subjects; orthostatic heart rates, although higher in both groups, increased significantly less in the test subjects. Following bedrest the incidence of syncope was significantly higher in the control subjects but was unchanged from before bedrest in the test subjects.

Hemodynamic cardiovascular measurements suggest that in response to acute sustained LBNP following bedrest, test subjects have a smaller increase in heart rate while the cardiac index decreases less than in the controls. Resting recumbent forearm blood flow is lower following 4 weeks of bedrest with LBNP than following bedrest alone. The increase in venous tone which occurs in response to acute exposure to LBNP is not apparant following pure bedrest but persists following bedrest with LBNP conditioning.

221. Stevens, P. M., P. B. Miller, T. N. Lynch, C. A. Gilbert, R. L. Johnson, and L. E. Lamb. Effects of lower body negative pressure on physiologic changes due to four weeks of hypoxic bedrest. *Aerospace Medicine* 37:466-474, 1966.

Authors' abstract: The effects of hypoxia and lower body negative pressure (LBNP) on blood volume, orthostatic and physical tolerance were studied in 22 subjects maintained at bedrest for 4 weeks at simulated altitudes of 10,000 and 12,000 ft. No significant differences in results were noted between the two altitudes. Hematocrits increased significantly by 7.2 percent. Plasma volume decreased (610-637 cc) while the calculated red cell mass either increased slightly or remained unchanged (133-89 cc). This suggests that hypoxia prevents the loss in red cell mass, but has no influence on the loss of plasma volume that occurs during bedrest on ground level; furthermore the erythropoietic response to hypoxia seems to be decreased by bedrest. A significant decrease in calculated red cell mass occurred during ambulation following bedrest but not during exposure to LBNP while at continued bedrest.

Exposure to LBNP during the last 2 days of bedrest repleted plasma volume and prevented subsequent orthostatic intolerance. In response to a given exercise load, the heart rate was much higher if the plasma volume was decreased but unchanged if the plasma volume was re-expanded by LBNP. Maximum oxygen consumption was decreased in all subjects following bedrest regardless of their blood volumes.

222. Stevenson, F. H. The osteoporosis of immobilization in recumbency. *Journal of Bone and Joint Surgery* 34B:256-265, 1952.

Purpose: To study the additional effect of bedrest on disturbances in bone growth.

Procedure and methods: Eighty-five patients were studied during or after immobilization without suspension for at least months of various diseases including tuberculosis, arthritis, and poliomyelitis.

Results: Prolonged immobilization, even when the limbs are entirely free from disease, produces both in children and adults gross radiographic changes in the lower limbs which clearly illustrate the disturbance of calcium metabolism. Ambulatory patients with long-standing subacute tuberculous arthritis have been seen who do not have osteoporosis.

Author's conclusion: While it is not denied that immobilization of a diseased joint may be essential, there is a growing mass of evidence that immobilization in recumbency of the whole patient has severe effects both in the neighborhood of the actual lesion and upon the skeleton as a whole. Further search for measures to counteract the undersirable skeletal effects of recumbency is much needed.

223. Storm, W. F. and C. L. Giannetta. Effects of hypercapnia and bedrest on psychomotor performance. *Aerospace Medicine* 45:431-433, 1974.

Authors' abstract: Two weeks of continous exposure to simulated weightlessness (bedrest) and/or an elevated (30 Torr) CO_2 environment had no detrimental effect on complex tracking performance, eye-hand coordination, or problem-solving ability. These results were consistent with previously reported behavioral findings which investigated these two factors only as independent stressors.

224. Strauss, M. B., R. K. Davis, J. D. Rosenbaum, and E. C. Rossmeisl. "Water diuresis" produced during recumbency by the intravenous infusion of isotonic saline solution. *Journal of Clinical Investigation* 30:862-868, 1951.

Authors' conclusions: Antidiuretic activity, ordinarily diminished by hypotonicity of the extracellular fluid, may also be diminished in the recumbent subject by isotonic expansion of the extracellular fluid volume. These results suggest that the receptors for expanded volume (or an associated factor) may have their locus in the cephalad portion of the body. Since the supra-optico-hypo physeal system is believed to be largely involved in the control of water excretion and since it is so located, it may be suggested that the receptor cells, known to respond to changes in osmotic pressure, may also respond to hydrostatic pressure.

The fact that an equal expansion of extracellular volume in the sitting subject does not significantly diminish antidiuretic activity, although there is an equal or greater expansion of both plasma and extracellular volume, suggests that the distribution as well as the magnitude of the expanded extracellular volume is of importance.

225. Syc, S. and A. Wedrychowski. Effect of immobilization on the urinary excretion of calcium. *Polskie Archivum Medycyny Wewnetrznez* 35:1621-1625, 1965.

Purpose: To investigate the 24-hr urinary calcium excretion in patients who were immobilized due to various internal diseases.

Procedure and methods: Twenty-four-hour urinary calcium excretion was measured in 17 men and 5 women (34 to 73 yr) who were immobilized for 21-32 days in bed. Eighteen of the patients were treated for a myocardial infarction, two for thrombophlebitis of the inferior extremities complicated by a pulmonary infarction, one for thrombophlebitis of the inferior extremities, and one for a myocardial infarction complicated by a pulmonory infarction. Three to five days before testing the patients received a calcium intake of about 105 mg/day.

Results: Among the 18 patients in whom complete data are available, the calcium excretion increased in 15 patients. In 10 cases the rise was more than 100 percent. Control calcium values averaged 115 mg/24 hr and the post-bedrest value was 259 mg/24 hr. Following bedrest the calcium level in the blood increased to 10.4 mg/100 ml from a pre-bedrest level of 9.7 mg/100 ml. The rise in urinary calcium was more pronounced among subjects who had previously been very active while those who were the least active showed little or no increased calcium excretion.

226. Syzrantsev, Yu. K. Effect of hypodynamia on nitrogen metabolism and importance of graded physical exercises for maintenance of the nitrogen balance. *Problemy Kosmicheskoy Biologii* 7:342-347, 1967.

Purpose: To study the changes in nitrogen metabolism during bedrest and water immersion with and without programs of physical exercises.

Procedure and methods: Nineteen subjects underwent up to five different experimental procedures: Group 1: Bedrest for 8 days, no exercise. Group 2: Water immersion for 8 days, no exercise. Group 3: Semibedrest for 10 days, isometric-isotonic exercise at 100 kcal/day. Group 4: Confinement in an environmental chamber for 30 days, isometric-isotonic exercise at 150-200 kcal/day. Group 5: Bedrest for 12 days, isometric-isotonic exercise at 400 kcal/day.

The diet was adequate and standard for each experiment.

Results: Urinary nitrogen excretion after bedrest was considerably increased in groups 1 through 4 and was unchanged in group 5. The greatest nitrogen excretion was found in the last days of each experiment.

Conclusions: A program of physical exercise at a level of 400 kcal/day is an effective means of maintaining the body protein.

227. Taylor, H. L., L. Erickson, A. Henschel, and A. Keys. The effect of bedrest on the blood volume of normal young men. *American Journal of Physiology* 144:227-232, 1945.

Authors' summary: The effect of 3 weeks of complete bedrest on the blood volume and its component parts has been studied in six experiments on five normal young men. In four men, studies were carried out during the course of reconditioning. In addition one of these men was studied before and after the surgical repair of an inguinal hernia. An average loss in blood volume of 572 ml or 9.3 percent occurred during the period of bedrest. This was almost entirely accounted for by a contraction of the plasma volume of 518 ml or 15.5 percent.

The first week of reconditioning resulted in an increase in plasma volume to pre-bedrest levels but was accompanied by an apparent loss of red cells so that the average increase of blood volume was only 235 ml. The subsequent apparent increase in blood volume to the original level was due entirely to an increase in red blood cells. The blood volume change after the surgical repair of an inguinal hernia and 3-week bedrest in one man did not differ significantly from the changes observed in the same man after simple bedrest alone. Correlations between blood volume changes and various indices of deterioration of cardiovascular function are discussed.

228. Taylor, H. L., A. Henschel, J. Brozek, and A. Keys. Effects of bedrest on cardiovascular function and work performance. *Journal of Applied Physiology* 2:223-239, 1949.

Purpose: To investigate the general nature of bedrest deconditioning, to what extent are the several fundamental components of fitness – coordination, speed, strength and endurance – affected by bedrest, and how rapidly do these components return to normal during the recovery period.

Procedure and methods: Six men (20 to 32 yr), of normal physical fitness, underwent a preliminary 6-week period of physical fitness, 3 weeks of bedrest, and 6 weeks of reconditioning. The preliminary conditioning program consisted of walking on a treadmill at 3.5 mph up a 10 percent grade and running for 3 min/day at 3 mph up a 10 percent grade for progressively longer duration and increasing number of runs over the 6-week period. They consumed 3400 to 3600 kcal/day, and as the conditioning program increased they ate 4400 kcal/day. During bedrest, the subjects were allowed to get up for 10 min/day and they were fed 2300 to 2600 kcal/day.

Measurements taken were: orthostatic tolerance, cardiac output, basal metabolism, maximal oxygen uptake, pattern tracing (coordination), ball pipe (speed of medium movements), tapping (speed of small hand movements), reaction time (speed of gross body movements), handgrip strength, back lift strength, ataxiameter, and heart size.

Results: Bedrest produced a 17-percent decrease in heart volume and an 8-percent decrease in the transverse diameter of the heart. There was a highly significant increase in the resting pulse rate which average roughly 0.5 beats/min for each day of bedrest. The pulse rate at the end of a half-hour walk at 3.5 mph and 10-percent grade increased by 40 beats/min after bedrest. There was no change in the mechanical efficiency during this walk, as the result of bedrest.

The oxygen intake during a 90-sec run at 7 mph and 15-percent grade was reduced by 730 cc of oxygen at 16 percent after 3 to 4 weeks of bedrest. This was accompanied by increases in oxygen debt and blood lactate after the run and a decrease in mechanical efficiency. The maximal oxygen intake was determined in two men who showed decreases of 13 and 22 percent after bedrest.

Bedrest produced a marked deterioration in the cardiovascular response to posture as measured by pulse rate and blood pressure changes produced by tilting to 68° on a tilt table. Ataxiameter studies showed that a definite increase in sway resulted from bedrest. Coordination, as measured by pattern tracing, suffered a small loss as the result of bedrest while speed of small hand movements, of medium arm and hand movements, and of gross body and arm movements showed no deterioration. Grip strength was not influenced by bedrest and back strength showed only a small deterioration.

After bedrest the rate of recovery of the various functions was roughly proportional to the extent of the deterioration in bedrest. Strength, coordination, and postural sway recovered early (4 days); blood lactate after exhausting work, and the oxygen cost of exhausting work recovered at an intermediate time (2 weeks); pulse rate during grade walking and O_2 intake during exhausting work recovered late (between 2 and 5 weeks), and the cardiovascular response to posture was very late in returning to normal (after 7 weeks). In one man the effect on the principal components of fitness of a herniorrhaphy with bedrest for 3 weeks was of the same order of magnitude as bedrest alone.

Conclusion: The major loss of performance resulting from bedrest deconditioning occurs within the cardiovascular system.

229. Tenney, S. M. Fluid volume redistribution and thoracic volume changes during recumbency. *Journal of Applied Physiology* 14:129-132, 1959.

Author's abstract: Continuous measurements of change in center of gravity, thoracic and abdominal girths, and extremity volume over a 30-min period of recumbency were recorded in 20 normal young adults. Vital capacity, expiratory reserve volume, and residual volumes were recorded at the beginning and end of the period. No significant differences between the initial and final vital capacities or residual volumes were observed. Expiratory reserve volume decreased and correlated positively with the measured change in torque. Abdominal and thoracic and expiratory circumferences both increased. Four young adults, normal except for congenital or traumatic absence of the lower extremities, were examined in the same manner. In these subjects the change in center of gravity was minimal and the thoracic circumference did not increase. The pattern of lung volume changes during recumbency was similar to normal subjects. It is concluded that during

recumbency the lower extremities contribute blood to the thoracic girth, but without decrease in total lung volume. The diaphragm assumes a more expiratory position and is partially responsible for the change in expiratory reserve volume.

230. Terent'Yev, V. G. The readaptation of the human organism after prolonged hypokinesia and the state of weightlessness. *Voyenno-Meditsinskiy Zhurnal* 3:53-56, 1972.

Abstract: The period of readaptation after prolonged bedrest or spaceflight can be divided into three phases:

Phase 1 (0 to 4 days): The change from the horizontal to the vertical position. Signs and symptoms: impairment of coordination during movements and standing, development of general asthenia and vascular-autonomic dystonia, an abrupt increase of pulse rate up to 100 or more beats per minute, an increase in systolic and diastolic pressures by 15 to 30 mm Hg, a reduction of pulse pressure, precomatose or comatose states during the orthostatic test, a reduction in tendinous and abdominal reflexes, muscular atrophy, decrease of muscle strength and tonus, mild euphoria, altered perception, that is, the size of a room seems to be larger and objects in it are relatively reduced in size.

Phase 2 (3 to 4 weeks): Development of myositis in the lower extremities, manifestations of pronounced asthenia and resting and exertion autonomic-vascular unsteadiness (tremor of the eyelids and fingers, hyperhydrosis, persistent dermographia and changes in the vascular-motor reflexes). Most of these manifestations disappeared in 3 weeks.

Phase 3 (2 to 3 months): continued unsteadiness of the autonomic-vascular indices during exertion tests (physical exercise, centrifugation). All impairments disappeared within 3 to 4 months.

During the recovery period the following procedure should be followed: There should be a gradual transition from lying to semireclining, to sitting, and then to the standing position. It may be necessary to place the astronauts in an immersion medium. Various restorative measures include therapeutic physical exercise, massage, hydrotherapy, and electrostimulation of the muscles. Physical exertion must be carefully regulated. During the first and second phases of recovery there is always the possibility of cardiac or cardiovascular insufficiency.

231. Tishchenko, M. I., B. A. Korolev, V. A. Degtyarev, and B. F. Asyamolov. Phase changes in the cardiac cycle during prolonged hypodynamia according to polycardiographic and kinetocardiographic data. *Problemy Kosmicheskoy Biologii* 13:59-64, 1969.

Purpose: To investigate the changes in the cardiac-cycle phase structure under the influence of hypodynamia, and to use the phase-analysis data for comparative evaluation of the effectiveness of various prophylactic measures taken to reduce or eliminate the influence of hypodynamia: physical exercises, occlusion cuffs, pharamceuticals.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

The phase structure of the cardiac cycle was studied under basal conditions and in subjects at rest after 30 min of relaxation. Measurements were carried out in the pre-bedrest period, daily during bedrest, and at the first, second, and fourth weeks after bedrest.

Conclusions: During 70 days of hypodynamia, a change in the phase structure of the cardiac cycle is observed in all subjects; the phase of blood expulsion and mechanical systole is shortened, the phases of tension, isometric contraction, and relaxation of the myocardium becomes longer, and the initial rise in rate of intraventricular pressure decreases.

The phase syndrome of hypodynamia is manifested equally in the control group and among subjects who engaged in physical exercise and occlusion conditioning and those who received medication. Normalization of the cardiac-cycle phase durations takes place only in the fourth week after hypodynamia.

232. Tizul, A. Ya. The function of thermoregulation in protracted limitation of motor activity (hypokinesia). *Zhurnal Nevropatologii i Psikhiatrii* 73:1791-1794, 1973.

Purpose: To study the effects of 120 days of bedrest on thermoregulatory function.

Procedure and methods: Ten healthy men (23 to 44 yr) were divided into three groups: group 1 (4 men) was the control, untreated bedrest group; group 2 (3 men) was given pituitrin and then deoxycorticosterone acetate (DOKSA); group 3 (3 men) was given the anabolic steroid nerobol. Temperatures were measured in the axilla, rectum, forehead, cheek, neck, chest, shoulder, back of the hand, abdomen, hip, skin, and top of the foot. Shcherbak's reflex test (measured each 15 days) was the rectal temperature response before and after immersing the arm in a water bath at 45°C for 10 min and then 30°C for 65 min. Also, the rectal temperature responses were measured after immersing the arm in a bath of 45°C for 30 min (Gauffe test). Subjective comfort reactions were recorded periodically.

Results: Complaints of a periodic sensation of temperature discomfort were made by all the subjects, most often by the three subjects in group I and by one subject in group II. The subjects complained of being chilled and of a feeling of coldness in the distal parts of the extremities, especially the legs. They often stated that they could not get warm. The subjective sensations of temperature discomfort appeared at the beginning of the second month and were accompanied by objective changes in the skin temperature.

Up to the end of the bedrest period and during the first 2 weeks of recovery, there was a sluggish response or absence of reactivity of the thermoregulation mechanisms in response to application of local thermal stimuli as well as by an increase in the restoration time of rectal temperature to control levels after elevation by heat stress.

The disturbances of the thermoregulation dynamics became more pronounced on the 45th day of bedrest; the thermal test resulted in virtually no reaction on the part of the thermoregulation system.

At the beginning of the second month of bedrest there was a clearcut tendency toward equalizing the differences in skin temperature between the trunk and extremities, chiefly as a result of elevation of temperature in the distal parts of the extremities. These responses were more distinct in groups I and II.

The administration of pituitrin and DOKSA in group II had no positive effect on thermoregulation while those who took nerobol (group III) exhibited a favorable effect on thermoregulatory responses. Restoration of normal thermoregulatory function occurred toward the end of the first month of ambulatory recovery.

233. Tizul, A. Ya., B. V. Kozlov, and G. V. Anan'yev. Cerebral hemodynamics during 120-day clinostatic hypokinesia. *Kosmicheskaya Biologiya i Medisina* 6:72-77, 1971.

Purpose: To investigate cerebral hemodynamics in 10 subjects during 120 days of bedrest.

Procedure and methods: Ten healthy men underwent 120 days of bedrest and a 21-day recovery period. They were divided into three groups: group 1 (4 subjects) – control group; group 2 (3 subjects) – injected with pituitrin for the first 30 days of bedrest and deoxycorticosterone acetate (DOCA) from the 70th to the 90th days; and group 3 (3 subjects) – given nerobol from the 1st to 28th and from the 70th to the 100th days of bedrest to help prevent possible impairments in protein metabolism.

Cerebral hemodynamic function was measured with a rheoencephalograph (REG) and orbital and temporal plethysmography; the latter recorded the pulse waves after occlusion of the cervical blood vessels. The REG was utilized once each 10 days in the first 60 days, once each 20 days during the last 60 days, and on the second and 20th days during recovery. The plethysmogram was taken once each 2 weeks.

Results: In the control group, the tone of the cerebral blood vessels was unstable during the entire bedrest period. Cerebral vessel tone was reduced during bedrest. There was less reduction in tone in the cerebral vessels of those subjects receiving pituitrin. The intensity of blood filling was reduced by 25 percent when pituitrin administration was stopped. The third group receiving nerobol showed the most stable pattern of blood filling and tone of the cerebral vessels during bedrest.

The plethysmographic changes were in the same direction as the REG changes, as mentioned above. During the first month of bedrest, there was a decrease in the reactivity of the extra- and intracranial vessels; the changes in the extracranial vessels were observed earlier. Only during the fourth month of bedrest was there some increase in the rate of emptying, especially of the orbital vessels: these results indicated a relative increase in the intracranial vessels and is indirect evidence of some compensatory adaptation.

Conclusions: Prolonged bedrest causes deterioration in cerebral hemodynamic function which includes a reduction in filling and decreased tone of the cerebral vessels.

234. Torphy, D. E. Effects of short-term bedrest and water immersion on plasma volume and catecholamine response to tilting. *Aerospace Medicine* 37:383-387, 1966.

Conclusions: The increased nitrogen loss during bedrest is not due to insufficient dietary protein. Dietary composition is important in helping to overcome the adverse responses to prolonged bedrest.

238. Umapathy, P. K. Effect of immobilization on urinary excretion of creatine and creatinine with certain possible ameliorating measures applied. Ph. D. Thesis, Texas Woman's University, Denton, Texas, Aug. 1967.

Author's summary and conclusions: Daily urinary creatine and creatinine excretion values were determined in two studies with human subjects and in one study with primates. These studies were conducted at the Texas Woman's University Research Institute under the sponsorship of the National Aeronautics and Space Administration. The analytical procedure used for determination of creatine and creatinine was the modified Folin method as described by Biggs and Cooper, and outlined in the Appendix of this dissertation.

The first study in this series consisted of two 14-day bedrest periods with and without planned isometric and isotonic exercises. Four adult male subjects participated in the first bedrest unit and two of these subjects remained for the second bedrest period. The exercises were repeated four times a day during bedrest 2.

The results showed that three of four subjects excreted significantly higher amounts of creatine during bedrest with no exercise than during the equilibration period. Although there was a considerable decline in the excretion of creatine following bedrest, the decrease was not significant for any of the subjects. On the other hand, creatinine excretion values exhibited less fluctuation from one period to another for each of the subjects. No statistically significant differences were obtained between bedrests 1 and 2 with regard either to creatine or creatinine excretion for the two subjects studied in the second bedrest.

In the second study of the series, an evaluation of the gravitation acceleration simulation suit designed by James Gatts, M.D., of the Republic Aviation Company, was carried out during a 21-day horizontal bedrest period in comparison with the same subjects during a similar bedrest period without the suit. This garment provided a workload both to the upper and lower body. All four adult men who took part in the study showed a highly significant decrease in creatine excretion during the period during which the suit was worn as compared to a similar period without the suit ($P < 0.001$). Also, the amount of creatine excreted while the suit was worn was not significantly different from that excreted during the pre-bedrest periods. The highest mean values were obtained for each of the subjects during the first bedrest. In regard to creatinine excretion, no statistically significant differences were obtained for the two bedrest periods, with and without the Gatts' suit.

In connection with this second study, however, it should be noted that the designer of the suit and a colleague supervised the men during the bedrest period when the suits were worn, rather than members of the TWU staff, with the level of recumbency maintained during bedrest periods of the TWU series including the bedrest period when the suits were not worn.

The third study in the series was conducted on six primates of the species Macaca nemestrina. The whole study was divided equally into three 14-day periods: equilibration, experimental, and recovery. Two monkeys served as controls, two were restrained without activity, and two were forced to exercise for 1 hr/day. Following the equilibration period of normal cage activity, two primates were immobilized in specially designed restraint couches and the second group was forced to exercise for 1 hr/day during this period. In the recovery period all the primates were allowed to have normal cage activity.

The results indicated that, during the equilibration period as well as the recovery period, there generally were not statistically significant differences between the three groups of monkeys with regard to the quantity of creatine excreted. As expected, the restrained monkeys excreted more creatine during the experimental period than did the other two groups of monkeys ($P < 0.001$ in each comparison).

During the exercise period, the exercised animals excreted less creatine than during the pre-exercise or the post-exercise periods. The difference in the first instance was statistically significant when the data for both primates in this group were pooled.

With regard to urinary creatinine excretion, the exercised animals excreted less creatinine during the exercise period than during the pre-exercise phase of the study, although the differences were not statistically significant. The same primates during the exercise period excreted far more creatinine than during the post-restraint period, probably because they were observed to exercise voluntarily in their cages for protracted periods of time after the supervised exercise period had ended.

The control animals did not excrete markedly different levels of creatine or creatinine during the various periods of the primate study.

The results of the above studies indicate that a suitable exercise program could prevent some of the undesirable physiologic and biologic changes that might occur during long space ventures.

Although creatinuria was reduced when the gravitation acceleration simulation suit was worn, the effect probably was due to a lesser degree of recumbency during the bedrest period when the suits were worn, as noted.

With respect to the second study of the period, it is probable that isometric and isotonic exercise might be more beneficial in reducing muscular atrophy during bedrest at earth gravity or during weightlessness in orbital flight if it were performed for longer periods of time or more frequently during the day.

239. Vallbona, C. Computer analysis of the effects of bedrest on cardiac dynamics. Symposium on the Analysis of Central Nervous System and Cardiovascular Data using Computer Methods. NASA SP-72. 1965, pp. 311-331.

Purpose: To quantitate the degree of cardiovascular deconditioning occurring as a result of 3 days and 14 days of bedrest; to test hypothesis on the mechanism of orthostatic hypotension; to evaluate data on the cardiac cycle and its phases; and to evaluate the effect of isometric exercises as a remedial procedure during bedrest deconditioning.

Results: During the 3- and 14-day bedrest periods, the duration of the cardiac cycle and the duration of systole and its isotonic and isometric phases oscillated at a 12-hr periodicity. In the 14-day study, the observed/predicted systole and isotonic phases of the heart were smaller in the evening, suggesting a circadian variation in the contractility of the myocardium with a positive inotropic effect in the evening hours resulting from adrenergic influences. There was a significantly higher urinary output of catecholoamines in the evening.

There was a significantly greater drop in mean blood pressure after 14-days bedrest without exercise compared with control values. The drop in mean blood pressure after 14-days bedrest with isometric exercise was not as great as without exercise. Therefore, isometric exercise provided some remedial effect on post-bedrest orthostatic tolerance.

All subjects who exhibited orthostatic hypotension after bedrest had a considerable increase in plasma 17-hydroxycorticosteroids during tilt.

240. Vallbona, C., F. B. Vogt, D. Cardus, W. A. Spencer, and M. Walters. The effect of bedrest on various parameters of physiological function, Parts 1 through 14.

Part I: Review of the literature on the physiological effects of immobilization. NASA CR-171, 1965.

Authors' abstract: A review of literature (up to 1963) on the effects of immobilization reveals that bedrest has been evaluated in 83 subjects (30 of whom were allowed to sit up) and water immersion in 33 subjects. There is a wide variety of experimental conditions in each study. This precludes pooling of data to evaluate the significance of the findings. It is concluded that bedrest deserves further study with special attention to include wider variety of subjects in regard to age, training habits, and physical condition; identification of physiological rhythms during bedrest; definition of changes in body composition; study of the mechanism of orthostatic hypotension following bedrest.

Part 2: Vallbona, C., F. B. Vogt, D. Cardus, and W. A. Spencer. Experimental design. NASA CR-172, 1965.

Authors' abstract: An Immobilization Study Unit was organized at the Texas Institute for Rehabilitation and Research under contract with the Manned Spacecraft Center of NASA to study the consequences of immobilization and its mechanisms. During 1963, a pilot experiment and two studies aimed at (a) quantifying cardiovascular deconditioning resulting from 3 days and 14 days of bedrest, (b) investigating the mechanisms of orthostatic hypotension, (c) evaluating indirect techniques of measurement of the cardiac cycle and its phases, (d) measuring bone demineralization, and (3) evaluating the effect of isometric exercises during bedrest in preventing deconditioning and demineralization. This report describes the study, the subjects, and the experimental conditions. The Appendix includes a master protocol and descriptions of techniques.

Part 3: Vogt, F. B., R. J. Lamonte, J. R. McConnell, T. O. Hallen, C. Vallbona, D. Cardus, W. A. Spencer, and T. W. Holt. Bioinstrumentation. NASA CR-173, 1965.

Authors' abstract: A bioinstrumentation system for collecting and recording multiple cardiovascular measurements was developed for use in tilt table tests and for bedside monitoring during bedrest studies. Each component unit of the system is discussed in this paper.

Part 4: Vallbona, C., W. A. Spencer, W. Blose, D. Cardus, F. B. Vogt, and J. Leonard. A system for processing data collected in the immobilization study unit. NASA CR-174, 1965.

Authors' summary: The establishment of the Immobilization Study Unit for the purpose of evaluating the physiological effects of bedrest required the provision of a system for processing, storing, and retrieving the data collected in the course of the studies.

A system was developed that permitted entries to punch cards of data pertaining to the subject's identification, past medical history, and physiological and sociological behavior during the study. Source documents of fixed format were used for collecting data at the bedside and in the laboratories.

Analog-to-digital conversion was achieved by means of manually operated automatic digitizers. Several computer programs were written that permitted application of mathematical and statistical models to the analysis of the data collected.

Part 5: Walters, M., C. Vallbona, D. Cardus, F. B. Vogt, and W. A. Spencer. Dietary requirements. NASA CR-175, 1965.

Authors' abstract: This report presents data of the nutritional intake of 13 subjects who participated in studies of the effect of short-term (3-day) and prolonged (14-day) bedrest. Two types of diets were used. One diet consisted of a 2-day cycle menu of fresh foods. The other consisted of three different menus of freeze-dried foods provided by the Food Research Division of the National Aeronautics and Space Administration. Freeze-dried foods were not as palatable to the subjects as fresh foods and some items were refused after the first time they were served. This offset the advantages of easy preparation of the freeze-dried meals and the small storage requirements of the packaged foods. The composition of the diets in terms of caloric, calcium, and nitrogen contents remained nearly constant throughout the studies. Prolonged bedrest did not produce a significant change in weight, but bedrest accompanied with isometric exercises resulted in a loss of weight in the majority of the subjects. There was no evidence of constipating effect of the low-residue diet provided by the freeze-dried foods.

Part 6: Vogt, F. B., D. Cardus, C. Vallbona, and W. A. Spencer. The effect of the performance of periodic flack maneuvers on preventing cardiovascular deconditioning of bedrest. NASA CR-176, 1965.

Authors' abstract: Six subjects participated in two 3-day bedrest periods: the first period consisted of bedrest alone, the second period consisted of bedrest plus periodic Flack maneuvers, and the periods were separated by 4 days to allow for recovery. At the end of the first period, three of six subjects experienced convulsive syncope while performing the Flack maneuver in the 70° tilt position. The subjects had not recovered at the start of the second period of bedrest. Repeated Flack maneuvers during bedrest did not prevent manifestation of orthostatism found with bedrest.

Part 7: Cardus, D., W. A. Spencer, C. Vallbona, and F. B. Vogt. Cardiac and ventilatory response to the bicycle ergometer test. NASA CR-177, 1965.

Authors' abstract: A study on effects of 14-day bedrest on tolerance to physical work was carried out on six healthy subjects. Tolerance was tested with the bicycle ergometer. Oxygen consumption, CO_2 production, pulmonary ventilation, breaths per minute, and frequency of the heart were measured at different workloads, and recovery time of heart rate after cessation of exercise. Results indicate that changes observed after 14-day bedrest in respiratory gas exchange, ventilation and mechanical efficiency were not significant; heart rate at rest and during exercise was significantly higher after 14-day bedrest. Isometric exercises carried out in a second 14-day bedrest period did not completely prevent the observed changes in heart rate.

Part 8: Vallbona, C., D. Cardus, F. B. Vogt, and W. A. Spencer. The effect on the cardiovascular tolerance to passive tilt. NASA CR-178, 1965.

Authors' abstract: This study was carried out to evaluate the effect of short-term (3-day) and long-term (14-day) bedrest on the cardiac tolerance to passive tilt. It showed that there was a deterioration of the subjects' ability to tolerate passive tilt. The deterioration was demonstrated by the negative slopes of the regressional line of blood pressure vs. time and the positive slopes of heart rate vs. time observed during tilt procedures at the end of the period of bedrest. The intolerance to tilt was more evident after bedrest for 14 days. This study showed also that isometric exercises performed while on bedrest improved the subjects' tolerance to passive tilt, as evidenced in the slopes of blood pressure, which although negative were less steep.

Part 9: Vallbona, C., W. A. Spencer, F. B. Vogt, and D. Cardus. The effect on the vital signs and circulatory dynamics. NASA CR-179, 1965.

Authors' summary: This study was carried out to evaluate if short-term (3-day) and long-term (14-day) bedrest would produce changes in the vital signs as well as in the duration of the cardiac cycle and its phases. A program of isometric exercises during bedrest was also evaluated to see if it would offset the possible cardiovascular effects of recumbency.

The results of this study showed that there were no obvious signs of circulatory "deconditioning" when bedrest lasted for 72 hr. There were circadian fluctuations in the duration of the various phases of the cardiac cycle, and it was concluded that under the conditions of this study the subjects were slightly under stress. This was more manifest in the second period of the study when a program of isometric exercises was introduced as an added variable. When bedrest was prolonged for a total of 14 days, the observations were in agreement with those of the first study, although there was a trend for the blood pressure to increase throughout the period of confinement. Circadian rhythms in the cardiac dynamics were also detected. The values of the systolic and isotonic ratios and of the pulse wave velocity suggest a slight degree of stress under the conditions of the experiment. The introduction of a program of isometric exercises during confinement to bed produced also changes in cardiac dynamics which are strongly suggestive to a greater reaction of stress.

Part 10: Vallbona, C., F. B. Vogt, D. Cardus, and W. A. Spencer. The effect of bedrest on the circulatory response to a Valsalva Maneuver. NASA CR-180, 1966.

Authors' abstract: Experimental design of studies of the effect of bedrest carried out at the Texas Institute for Rehabilitation and Research in 1963 included an evaluation of the performance of a controlled Valsalva maneuvar before and after bedrest. This report presents the quantitative results of the changes in arterial blood pressure during the performance of a controlled Valsalva maneuver before and after bedrest by a group of 13 individuals who participated in this study. An analysis of the data indicates that after 14 days of bedrest the Valsalva maneuver may trigger a greater adrenergic reaction to compensate for the decreased venous return in the phase of forced expiration. This adrenergic reactions was evident also in subjects who developed poor tolerance to passive tilt following bedrest. The findings suggest that a mechanism of orthostatic hypotension after bedrest must be explained on the basis other than deficit in the autonomic nervous system of these individuals.

Part 11: Vogt, F. B., W. A. Spencer, D. Cardus, and C. Vallbona. The effect of bedrest on blood volume, urinary volume, and urinary electrolyte excretion. NASA CR-181, 1965.

Authors' abstract: Seven subjects participated in 14-day bedrest studies using controlled diets and careful measurement of intake and output. A 14-day bedrest period was followed by a 14-day recovery period, which in turn was followed by a second 14-day bedrest period to which was added an exercise program. A diuresis and naturesis was observed with bedrest. Day-to-day variation in plasma volume determination makes interpretation of this measurement difficult.

Part 12: Vogt, F. B., P. B. Mack, W. G. Beasley, W. A. Spencer, D. Cardus, and C. Vallbona. The effect of bedrest on bone mass and calcium balance. NASA CR-182, 1965.

Authors' abstract: Seven subjects participated in 14-day bedrest studies using approximately 1.0-gm calcium diets. A 14-day bedrest period was followed by a 14-day recovery period, which in turn was followed by a second 14-day bedrest period to which was added an isometric exercise program. The exercise program appeared to prevent the loss of bone density which occurred in the bedrest without exercise period. Calcium balance results are difficult to interpret because of short control periods to attain an equilibrium to the test conditions.

Part 13: Vogt, F. B., W. A. Spencer, D. Cardus, and C. Vallbona. A review of possible mechanisms of orthostatic intolerance to passive tilt. NASA CR-183, 1966.

Authors' abstract: The review includes a discussion on bedrest and water immersion studies and relates the observations which have been reported in the literature on certain features of cardiovascular function, intravascular volume, and transfer of fluid and electrolytes into and out of the intravascular volume, and transfer of fluid and electrolytes into and out of the intravascular system to define a possible mechanism accounting for some features of "cardiovascular deconditioning" manifested in the passive tilt procedure. Experimental procedures are suggested which would test the validity of this hypothesis. It is concluded that future bedrest studies should be directed to defining more precisely the mechanism involved to account for the changes in tilt response after bedrest compared to those observed before bedrest.

Part 14: Cardus, D., C. Vallbona, F. B. Vogt, W. A. Spencer, H. S. Lipscomb, and K. B. Eik-Nes. Effect of bedrest on plasma levels and urinary excretion of 17-hydroxycorticosteroids, NASA CR-184, 1965.

Authors' abstract: Plasma levels of 17-hydroxycorticosteroids at 0800, 1200, 1600, 2000 and 2400 hr were determined on six healthy subjects who were submitted to bedrest for 3 days. The determinations were made with a modification of the Peterson method and the Porter-Silber technique. During bedrest the peak level at 0800 seemed a little lower than normal, but the circadian rhythm of 17-hydroxycorticosteroids was not modified. During bedrest and isometric exercises, the rhythm and the levels of 17-hydroxycorticosteroids were normal. Relatively short periods of physical inactivity seem to have no effect on the circadian rhythm of 17-hydroxycorticosteroids.

241. Vasil'Yev, P. V. and B. Yu. Lapinskaya. Results from use of medication in individuals subject to prolonged hypokinesia. *Problemy Kosmicheskoy Biologii* 13:206-214, 1969.

Purpose: To study the effect of drugs that stimulate the compensatory-adaptive reactions of the organism for the prevention of hemodynamic disturbances during bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Drug administration was carried out during the pre-bedrest period, on the 15th and 53rd days of bedrest in group II, on the 67th day of bedrest in groups IV and V, and on the 16th day of the recovery period. All subjects in groups II, IV, and V received the medication 1 hr before the orthostatic test.

Authors' summary: The influence of prolonged hypokinesia on the reactivity of the organism with respect to a combination of medications (amphetamine, securinine, caffeine) and the possibility of improving human tolerance to orthostatic loads and the action of transverse G-forces with the aid of these drugs were studied in experiments in which 11 subjects participated.

It was established that the action of the medication changed under hypodynamia: in most cases, the effect was weaker and inversion occurred in a number of observations.

As a rule, tolerance of orthostatic loading and G-forces increased following administration of the above agents, expecially when they were given to individuals who performed a set of physical exercises.

In all cases, the decrease or increase in the subjects' stability after hypodynamia was arrived at with considerably greater stressing of the organism's functional systems than was observed before hypokinesia.

242. Vernikos-Danellis, J., C. S. Leach, C. M. Winget, P. C. Rambaut and P. B. Mack. Thyroid and adrenal cortical rhythmicity during bedrest. *Journal of Applied Physiology* 33:644-648, 1972.

Authors' abstract: The effects of prolonged bedrest on adrenocortical and thyroid function were assessed in eight healthy males, aged 20-40 yr, who were submitted to bedrest for 56 days on a 14L:10D regimen (lights-on, 9:00 a.m.). Four of these subjects exercised with an Exergenie three times daily throughout the experiment. Circulating cortisol, triiodothyrinine (T_3), and thyroxine (T_4) concentrations were determined in blood samples drawn at four hourly intervals for 48-hr periods before, 10, 20, 30, 42, and 54 days during, and 10 days post-bedrest. Significant fluctuations in the circulating levels of all three hormones occurred with peaks at 7:30 a.m. Bedrest reduced the amplitude of the cortisol rhythm but the rhythm persisted. In contrast, thyroid hormone rhythms were considerably less stable during bedrest, showing marked rephasing with progressive bedrest, and returning to original rhythmicity at the 10-day post-bedrest sampling period. The mean daily concentration of T_3 increased promptly during bedrest and remained elevated. Neither exercise nor the 10-day post-bedrest ambulatory period prevented or corrected these effects. The suggestion is advanced that thyroid rhythms may be posture-dependent.

243. Vernikos-Danellis, J., C. M. Winget, C. S. Leach, and P. Rambaut. Circadian, endocrine, and metabolic effects of prolonged bedrest: Two 56-day bedrest studies. NASA TM X-3051, 1974.

Authors' abstract: Two bedrest studies of 56 days each, involving a total of 20 male subjects aged 20-26 (one subject aged 40), have been conducted to evaluate the effects of prolonged bedrest on circadian synchrony and endocrine and metabolic function. Measurements included the pituitary-adrenal, thyroid, parathyroid, insulin-glucose-growth hormones, catecholamine excretion, body temperature, and heart rate. The results indicate that a rigorous regimen of isotonic/isometric exercise did not prevent the endocrine and metabolic effects of prolonged bedrest. Changes in circadian, endocrine, and metabolic functions in bedrest appear to be due to changes in hydrostatic pressure and lack of postural cues rather than to inactivity, confinement, or the bleeding schedule. Changes in circulating metabolic and endocrine parameters are unreliable if measured once per day because their amplitude and time of peak of their diurnal fluctuations are altered during bedrest. Therefore, data should be expressed as units/24 hr. Recovery periods up to 20 days are insufficient for full recovery from 56 days of bedrest. Bedrest beyond 42 days results in periodic hypoglycemia, possibly in response to meals, which may warrant modification of meal composition.

Prolonged bedrest, particularly beyond 24 days, results in rhythm desynchronization in spite of well-regulated light/dark cycles, temperature, humidity, activity, and meal times and meal composition and in increased lability of all endocrine parameters measured.

It also results in an apparent insensitivity of the glucose response to insulin, of cortisol secretion to ACTH, and of growth hormone secretion to hypoglycemia. This may be due to an effect of bedrest on the number or sensitivity of target organ receptors; it may reflect a change in radio-immunoassayable levels of the peptide hormones, or it may result from an alteration of the central nervous system's input/feedback integrating mechanisms.

244. Vetter, W. R., R. W. Sullivan, and K. H. Hyatt. Deterioration of left ventricular function; a consequence of simulated weightlessness. Aerospace Medical Association Preprints, 1971, pp. 56-57.

Purpose: To correlate results of apex cardiography (ACG) with results obtained by cardiac catheterization and left ventricular angiography and to study the direction, magnitude, and duration of ventricular function alteration occurring during bedrest.

Procedure and methods: Eleven young male volunteers on metabolic diets, undergoing concomitant assessments of body fluid volumes, were studied prior to, on the last day of, and at 2 and 3 weeks following 4 weeks of absolute bedrest. Apex cardiograms, recordings of the apical left ventricular displacement, were performed. The R to dA/dt interval was measured for 12 cardiac cycles and the mean value reported.

Diagnostic cardiac catheterization and ACG's were performed on 23 additional patients. Intracardiac pressures are referred to the midchest level and cardiac output was measured by the direct Fick principle. The first derivative of left-ventricular pressure was obtained electrically from measurements through well-flushed catheters with Statham P23Dd transducers. Vmax was calculated using simultaneous left-ventricular pressure and its first derivative.

Left-ventricular angiograms were filmed at 64 frames/sec in the right anterior oblique position for volume determination. Angiographic stroke volume and ejection fraction was calculated.

Results: Among the 11 normal volunteers studied before and after bedrest, all but one showed increases in R to $dA/dt/\sqrt{RR}$, suggesting deterioration of left-ventricular function. The changes which took place during simulated weightlessness were statistically significant and did not resolve until 3 weeks of re-ambulation had elapsed.

Conclusion: By a technique of quantitative apex cardiography, shown in this study to reflect left ventricular function, changes were observed during 4 weeks of simulated weightlessness which suggest that ventricular function deteriorated. This is consistent with findings from earlier studies showing a decrease in cardiac output response to exercise following bedrest. The duration of the changes observed in this study is greater than that of the previously noted fluid volume changes, which resolve in general during the first week of re-ambulation.

245. Vinogradov, V. N., V. G. Petrukhin, and I. V. Fedorov. Morphological changes produced in animal organs by prolonged hypodynamia and subsequent physical exertion. *Byulleten' Eksperimental' noi Biologii i Meditsiny* 65:96-99, 1968.

Purpose: To investigate the early structural changes that develop in the organs and tissues of rats during immobilization.

Procedure and methods: Thirty albino rats were kept for 15 days in plaster casts. Subsequently, 6 of these rats were made to swim for 30 min. Twelve rats and 2 dogs were confined in small cages for 100 days and subsequently subjected to radial acceleration.

Summary: Restriction of mobility of rats for 15 days leads to atrophy of skeletal muscles, an increase in the weight of the adrenal glands, a decrease in the glycogen reserves of the body, and an increase in succinate dehydrogenase activity, and a decrease in alkaline phosphatase activity in the liver. The resistance of the animals to swimming and radial acceleration is lowered in animals after immobilization and confinement, and more marked morphological deterioration is found in the myocardium, lungs, and liver than in control animals.

Conclusions: These results are in accord with the conclusion that immobilization results in the depression of synthesis reactions in the organism.

246. Vogel, J. M. A study of bone mineral content performed by the gamma ray absorption technique in prolonged bedrest subjects maintained in a metabolically controlled environment. NASA CR-108, 316, 1970.

Author's summary: A method of estimating the mineral content of a large volume of the os calcis by scanning with a monoenergetic photon source and observing the degree of photon absorption has been described.

The degree of reproducibility of scan data as well as repositioning has been found to be most satisfactory in following the bone mineral content changes in a group of subjects for 42 to 60 weeks. Bone mineral loss from the central os calcis during a 30-36-week period of bedrest is substantial – 26.9, 36.7, and 53.5 percent in the three subjects. Areas with the least bone mineral at the beginning of the study lost it more rapidly during bedrest and regained it more rapidly after reambulation than areas with greater mineral content. The subject with the least total bone mineral lost the most and, conversely, the one with the most lost the least.

The os calcis, a bone repetitively subjected to full body weight stresses, can be placed at risk after return to G conditions if these substantial mineral losses occur during a prolonged period of weightlessness.

247. Vogt, F. B. Effect of intermittent leg cuff inflation and intermittent exercise on the tilt table response after ten days bed recumbency. *Aerospace Medicine* 37:943-947, 1966.

Author's abstract: Eleven healthy adult male subjects were studied using tilt-table procedures before and after three 10-day periods of recumbency. Intermittent cuff inflation on the lower extremities or periodic exercise procedures were performed during each of two periods of recumbency. Definite cardiovascular deconditioning as manifested in statistically significant changes in the tilt-table response was observed after each recumbency period. No statistical difference was observed in the comparison to the response to each recumbency period with that in which a potential treatment was added. Tilt-table responses of nonathletes differed from athletes prior to deconditioning, but the trend of change with deconditioning was similar.

248. Vogt, F. B. Tilt table and plasma volume changes with short term deconditioning experiments. *Aerospace Medicine* 38:564-568, 1967.

Authors' abstract: The tilt-table response of nine experimental subjects was evaluated before and after short-term periods of deconditioning, including chair rest, bedrest, water immersion, and water immersion with cuffs. Twelve-hour deconditioning experiments were conducted utilizing the following eight experimental conditions: (a) water immersion, (b) water immersion, arm cuffs only, (c) water immersion, leg cuffs only, (d) water immersion, arm and leg cuffs, (e) bedrest, (f) chair rest, (g) water immersion with leg cuffs the last 4 hr, and (h) water immersion with leg cuffs 15 min/hr. In water immersion experiments, the subjects were immersed in a sitting position, head out, with a water temperature of 94°F. Cuffs were inflated in cycles, with inflation to 70 mm Hg for 2 of every 6 min. The results indicate that definite cardiovascular deconditioning occurred with water immersion, as evidenced in the plasma volume decline and the tilt-table response. There was a significant decline in plasma volume during all experimental conditions except chair rest. The results of this study do not indicate a definite protective effect from the use of intermittently inflated extremity cuffs.

249. Vogt, F. B. and P. C. Johnson. Plasma volume and extracellular fluid volume changes associated with 10 days bed recumbency. *Aerospace Medicine* 38:21-25, 1967 (also Proceedings of the 2nd Annual Biomedical Research Conference, Manned Spacecraft Center, Houston, Texas, Feb. 17-18, 1966).

Authors' abstract: Eleven healthy adult males were studied before, during, and after three periods of 10-days recumbency. Intermittently, inflated cuffs were applied to the lower extremities or periodic exercises were performed by the subjects during two of the three periods of recumbency. A significant decrease in plasma volume occurred in the first several days of recumbency. Extracellular fluid volume decrease was progressive over the recumbency period. The use of intermittent cuff inflation on the lower extremities or periodic exercises did not influence the plasma volume and extracellular fluid volume change seen in association with 10-day bed recumbency.

250. Vogt, F. B. and P. C. Johnson. Effectiveness of extremity cuffs or leotards in preventing or controlling the cardiovascular deconditioning of bedrest. *Aerospace Medicine* 38:702-707, 1967.

Authors' abstract: Six young healthy adult male subjects were studied during three 14-day periods of bedrest with the experimental conditions of bedrest, bedrest with armcuffs, and bedrest with armcuffs and leg cuffs. The inflation-deflation cycle for the extremity cuffs was 2-min on, 4-min off, with an inflation pressure of 70 mm Hg. Tilt-table and plasma volume studies were performed on the subjects before and after each 14-day period of deconditioning. The tilt procedure consisted of two consecutive tilts performed on each subject before and after bedrest, with the subject wearing leotards for the first tilt followed by a tilt without the use of leotards. The use of extremity cuffs was confined to the period of deconditioning only. The studies indicate that after deconditioning has occurred, the use of leotards on the subjects provides a protective effect against the tilt-table manifestations of cardiovascular deconditioning. A significant protection was not observed with the use of intermittently inflated extremity cuffs during bedrest.

251. Vogt, F. B., P. B. Mack, and P. C. Johnson. Tilt table response and blood volume changes associated with thirty days of recumbency. *Aerospace Medicine* 37:771-777, 1966.

Authors' abstract: Five healthy adult males were studied during a 30-day bedrest experiment. Repeated tilt-table tests, using an English saddle type of support, were conducted before and after the period of recumbency to determine the response of the subjects. Radioisotope blood volume determinations were made prior to the study, during the study, and during the recovery phase. These tests were performed in conjunction with a study designed primarily to evaluate the musculoskeletal changes that occur as a consequence of prolonged bedrest. The results indicate that definite cardiovascular deconditioning occurs after 30 days of bedrest and that almost complete recovery is achieved after 2 weeks of ambulatory activity. The study also demonstrates that blood volume decreases in the first few days of bedrest and returns toward normal at the end of the 30-day bedrest period.

252. Vogt, F. B., P. B. Mack and P. C. Johnson. Effect of garments which provide work loads in preventing the cardiovascular deconditioning of bedrest. *Aerospace Medicine* 38:1134-1137, 1967.

Authors' abstract: Five healthy adult male subjects participated in two successive bedrest periods of 3-weeks duration to evaluate the potential protective effect of exercise garments in preventing the cardiovascular deconditioning associated with prolonged bedrest. During the first period of bedrest, the subjects underwent a period of inactive bedrest during which they remained flat in bed. During the second period of bedrest, the subjects wore a specially fitted suit to provide an exercise load to the musculoskeletal system. The results of the studies indicated no statistically significant difference in the cardiovascular response after the two bedrest conditions.

253. Vogt, F. B., P. B. Mack, P. C. Johnson, and L. Wade, Jr. Tilt table response and blood volume changes associated with fourteen days of recumbency. *Aerospace Medicine* 38:43-48, 1967.

Authors' abstract: Four healthy adult males were studied during a 14-day bedrest experiment. Repeated tilt-table tests, using an English saddle type support, were conducted before and after the period of recumbency. Particular attention was directed during the post-recumbency period to the determination of the pattern of the subjects' tilt-table response in recovering from the 3-day recovery period following recumbency. Radioisotope blood volume determinations were made prior to the study, during the study, and during the recovery phase. The results indicate that definite cardiovascular deconditioning occurred after 14 days of bedrest, and that significant recovery is attained with 3 days of ambulation. The study demonstrated that blood volume decreases in the first several days of bedrest, without a further statistically significant change during the remainder of the 14-day period of bedrest. Also discussed are the discrepancies in determining plasma volume by counting plasma directly, and by determining plasma volume from calculations using total blood volume (obtained by counting whole blood) and its associated hematocrit reading.

254. Voloshin, V. G., I. D. Pestov, and B. F. Asyamolov. Occlusion conditioning under the conditions of prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:200-205, 1969.

Purpose: To evaluate the use of blood flow occlusion on cardiovascular dynamics during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

This occlusion procedure was applied in the 4th, 7th, and 10th weeks for 3 hr in the morning, afternoon, and evening on an every-other-day sequence. Thus, each subject received occlusion conditioning on 4 days/cycle or for a total of 12 days during the course of the experiment (a total of 108 hr).

Conclusions: There was no clear evidence that the occlusion conditioning was beneficial.

255. Vose, G. P. and L. M. Hurxthal. X-ray density changes in the human heel during bedrest. *American Journal of Roentgenology* 106:486-490, 1969.

Authors' summary: In a study of the effects of recumbency on bone density, three young adult males participated in a study involving 14 days of complete bedrest, and one subject was retained as an ambulatory control.

A slight but significant increase in x-ray density at the os calcis site was noted among the bedrest subjects as the study progressed, but the increase was not evident in the control subject. No significant density variations occurred in the hand phalanx or distal radius.

Periodic caliper measurements of the heel indicated that increased tissue thickness during the latter phases of bedrest may have accounted for the apparent gain in x-ray density of the os calcis. Such an increase in tissue thickness may be a result of venous pooling in the limbs with immobilization.

An adequate soft-tissue correction factor must be applied in future studies of the effects of bedrest and weightlessness upon skeletal density.

256. Voskresenskiy, A. D., B. A. Korolev, and M. D. Ventsel'. Changes in electrocardiogram and statistical structure of cardiac rhythm in the course of confinement to bed. *Problemy Kosmicheskoy Biologii* 13:35-44, 1969.

Purpose: To study the EKG records obtained under basal conditions during prolonged bedrest.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were given treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day.

These two groups were also given orthostatic tolerance tests on a tilt table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Authors' summary: Analysis of EKG recorded during a 7-day confinement to bed showed position changes, relative inhibition of conduction, decreased amplitude of the R and T deflections, a change in the relationship between the T from various leads, a periodic displacement of the S-T segment, and changes in the repolarization process for all of the subjects. These shifts appeared later and were less consistent in subjects who performed a set of physical exercises.

Correlation functions calculated for series of 200-300 successive values of the R-R interval revealed a picture of respiratory-arrhythmia decay and the appearance of undulating variations of the rhythm that were not related to respiration. The R-R correlation functions showed little change from their original form in the individuals who performed physical exercises.

257. Voskresenskiy, A. D., B. B. Yegorov, I. D. Pestov, S. M. Belyashin, V. M. Tolstov, and I. S. Lezhin. Organization of the experiments and overall condition of the subjects. *Kosmicheskaya Biologiya i Meditsina* 6:28-32, 1972 (same basic study as those reported by Drozdova *et al.*, 1972; Pestov *et al.*, 1972; Yarullin *et al.*, 1972; Balakhovskiy *et al.*, 1972; Stepantsov *et al.*, 1972; Katkovskiy *et al.*, 1972; Genin *et al.*, 1972; and Pometov *et al.*, 1972).

Purpose: To investigate the influence of various remedial procedures upon subjects during 30-day horizontal bedrest and during bedrest with the bed tilted 4° downward.

Procedure and methods: Series A – group 1 (three subjects 19 to 20 yr): bedrest in the horizontal position for 30 days and LBNP twice a day for 6 hr/day. Series A – group 2 (three subjects 19 to 20 yr): bedrest in the horizontal position; from the 26th to 30th day LBNP for 2.5 hr/day at pressures of −50 to −55 mm Hg. The subjects ate a hospital diet of 3200 to 3400 kcal/day. Series B – group 1 (three subjects 19 to 21 yr): bedrest for 30 days with the head tilted downward 4°. Vertical treadmill isotonic exercise for 1 hr/day. From 26th through 30th days isotonic exercise plus LBNP for 2.5 hr/day at −36 to −44 mm Hg. Series B – group 2 (three subjects 24 to 29 yr): no-exercise control group. Series B – group 3 (three subjects 25 to 33 yr): daily electric stimulation of muscles of lower leg, hip, abdomen, and back for two 30-min periods daily. The subjects ate a special diet composed of preserved foods, about 3200 kcal/day. In all experiments water comsumption was unrestricted.

In series B, orthostatic tolerance was measured four times during 10-min LBNP tests.

Results: Series A: During the first 7 to 10 days, the subjects continued to feel well. Complaints of postural discomfort were customary. All subjects in group 1 exhibited symptoms of emotional lability, irritability, and rapid fatigability. Sleep and appetite deteriorated and they periodically complained of headaches. The LBNP testing became very tiring. In group 2, when the LBNP applications began, the general apathy and malaise symptoms decreased. In group 1 body weight decreased by 2.83 kg (1.0 to 4.0 kg) and in group 2 the decrease was 1.7 kg (1.2 to 2.1 kg). There was no change in weight 5 days after bedrest. No complete restoration of the feeling of well-being had occurred after 10 days of recovery. Increased fatigability persisted up to 1 month after bedrest.

Series B: Immediately after assuming the 4° head-downward position, the subjects sensed increased blood flow to the head, together with pulsations in the temporal regions. These sensations reached maximal intensity approximately 3 hr after assuming the position. Two subjects complained of increased thirst sensations on the first day. All subjects exhibited hyperemia of the facial skin. Some symptoms persisted up to 15 days. When falling asleep, some subjects suffered from shortness of breath. Appetite was satisfactory throughout the 30-day bedrest period. One hour of physical exercise and 2.5 hr of LBNP were well tolerated by the subjects. Electric stimulation had a favorable effect on the feeling of well-being of the subjects, but by the end of the experiment there was a sensation for a need to exercise the muscles, particularly in the morning. Group 1 lost 1.93 kg (0.2 to 3.35 kg); group 2 lost 3.08 kg (2.25 to 4.25 kg), and group 3 lost 2.17 kg (1.0 to 3.0 kg). All subjects stated that 3 days after bedrest they felt entirely well.

Conclusions: Daily LBNP training for a 6 hr/day at −30 mm Hg creates adverse symptoms. Application of LBNP only during the last 5 days of bedrest is more acceptable. Since LBNP partially or completely prevents loss of plasma volume, perhaps the malaise and other untoward symptoms present with daily LBNP are due to "hyperhydration," by not allowing the body to lose fluid volume. Assumption of the 4° head downward position appears to be a more adequate simulation of weightlessness than the usual horizontal position. Physical exercise and the application of LBNP during the last 5 days of bedrest ensures a more effective counteraction of the general asthenia.

258. Vyazitskiy, P. O. and S. D. Kumanichkin. The effect of hypodynamia on external respiration under various microclimatic conditions. *Voyenno Meditsinskiy Zhurnal* 7:38-40, 1970.

Purpose: To investigate the respiration function of man under the influence of hypodynamia in various microclimatic conditions.

Procedure and methods: Eight young healthy males (20 to 24 yr) were subjected to 6 days of hypodynamia in various microclimatic conditions. During the hypokinesis the test subjects were kept in a sitting position in a small chamber in a comfortable temperature, in a hot, humid microclimate (air temperature – 35° and relative humidity 90 percent) and in a temperature of +8°. The air-ventilation rate in all cases did not exceed 0.4 m/sec.

The following data were determined in their initial condition and after they left the chamber by the use of Belau's apparatus, vital capacity, oxygen consumption level at rest, respiratory minute volume, increasing oxygen consumption at work, oxygen debt after work, oxygen requirement for a given type of work, relative oxygen debt, the half-life period of adaptation and restoration, and oxygen consumption per unit of work. All the test subjects both in their initial condition and when they left the chamber following the determination of the functional restoration indices were under the same physical load (200 kg-m/min for 5 min).

Results: The following was noted by the end of the investigation: a reduced pulse frequency (by an average of 14 beats/min), a lower pulse blood pressure (by an average of 11 mm Hg), and a lower stroke volume of the blood (by an average of 6 ml). The peripheral blood resistance, on the other hand, increased. There was also a change in the phasic structure of the cardiac cycle. The subjects themselves noted that their manual work required considerably greater efforts than before the experiment. This subjective evaluation was confirmed by a number of objective data: an increase in the consumption of oxygen under a physical load and a growing oxygen deficiency after it. Their capacity for work was not fully restored even 10 days after the experiment.

Conclusions: Hypodynamia under various microclimate conditions is not conducive to a reduced permeability of the diffuse lung membrane. The functional respiratory indicators under a physical load after hypodynamia in comfortable microclimatic conditions are subject to the most pronounced changes. A thorough analysis of the changes on the part of individual respiratory indicators reveals that they are determined by the condition of the cardiovascular system.

259. Warren, B. H. A comparison of physiological changes occurring during water immersion and bedrest. *Aerospace Medicine* 34:268, 1963.

Author's abstract: Human water immersion experiments have been performed by several investigators under the assumption that the resulting "hypodynamic" environment simulates certain conditions of weightlessness. Bedrest has also been used as a method for studying the hypodynamic state. In the present investigation a controlled comparison of these techniques was made. Twelve healthy male volunteers took part in these experiments. Each subject was studied during two 6-hr water immersion periods and one 6-hr bedrest period. Physical and psychological variables were kept as constant as possible. Electrocardiograms were traced continuously and blood pressures were recorded automatically. Blood and urine samples were collected for physical and chemical determinations. A tilt table was used to produce gravitational stress for measuring cardiovascular responses before and after each hypodynamic period. An analysis of the data revealed that the direction of change of a physiological parameter during water immersion coincided with the direction of change of the same parameter during bedrest. The biological relationship of the above hypodynamic factors to weightlessness can only be hypothesized. Further evaluation of physiological changes occurring during water immersion and bedrest appear warranted, however, before either is accepted as a better tool than the other for studying the hypodynamic state in man. In over 30 hypodynamic periods above, no significant differences were noted in the physiological parameters measured during water immersion and bedrest which could not be attributed to factors other than an increased hypodynamic state during water immersion.

260. Whedon, G. D. Effects of weightlessness on mineral metabolism: Experience to date. *Astronautica Acta* 17:119-128, 1972.

Author's abstract: Prior to the first actual measurements in space flight, predictions as to the effect of weightlessness on mineral metabolism were based mainly on studies of the effects of physical immobilization or bedrest, the nearest simulation to weightlessness for ground-based observation: water immersion studies could be continued for too short a period to reveal possible effects on the skeleton. Immobilized bedrest studies have shown a negative calcium balance and a gradually increasing urinary calcium excretion up to 5 weeks, to as much as two to three times the control level, followed by a plateau continuation of loss thereafter. Inactivity due to paralytic poliomyelitis revealed a similar pattern of calcium loss with some decrease in rate of loss after 2 months; the first indication of bone loss by conventional x-ray appeared in bones of paralyzed legs at 3 months.

First efforts to assess mineral loss in spaceflight were made by bone densitometry of the os calcis before and after Gemini flights IV, V, and VII. With this technique apparent losses ranging from 6 to 23 percent occurred in a bone which is not representative of the whole skeleton.

The first comprehensive effort to measure mineral metabolic changes by metabolic balance technique took place in conjunction with flight Gemini VII. The study involved dietary intake control and collections of all excreta before, during and after this 14-day flight. Among the many elements measured, modest but significant clacium loss occurred with interindividual differences. The changes in calcium and electrolyte metabolism observed probably represented the composite effect of several different, concurrent, and counteracting physical influences.

Studies are currently needed on the ground to dissect out the effects of hyperoxia, diminished atmospheric pressure, and other factors. Future long spaceflights will need to include metabolic studies to determine clearly the effects of weightlessness on mineral metabolism, a potential problem of serious significance on flights of several weeks or more.

261. Whedon, G. D., J. E. Deitrick, and E. Shorr. Modification of the effects of immobilization upon metabolic and physiologic functions of normal men by the use of an oscillating bed. *American Journal of Medicine* 6:684-711, 1949.

Purpose: To determine the effectiveness of an oscillating bed for use in bedridden patients with diseases where the usual convalescent training methods are unsuitable.

Procedure and methods: Three normal healthy men (21 to 30 yr) underwent a 28- to 35-day ambulatory control period, 35 days in bed encased in a bivalved plaster cast extending from the umbilicus to the toes and a recovery period of 35 to 45 days. After recovery one subject, S. W., was again immobilized for 14 days in a fixed bed. The subjects were taken out of the casts between 30 and 45 min/day for bowel movements, tilt-table, and ergometer testing. All three subjects received 2800 kcal/day and sodium intake was 4.0 gm/day.

Chemical analyses made were urinary and fecal calcium, phosphorus, citric acid, nitrogen, sulfur, potassium, sodium, urinary creatine, 17-ketosteroids, specific gravity; and blood prothrombin time, heparin tolerance, total proteins, phosphorus, sodium coagulation and potassium; serum calcium; basal metabolism, muscular strength, limb girth, orthostatic tolerance, blood volume, circulation time, exercise tolerance, heart size, EKG, hematocrits, and the psychological condition of the subjects.

Authors' summary: A study was made of the influence of an oscillating bed on the metabolic and physiologic disturbances associated with immobilization. The subjects were three normal healthy young men. The investigation was carried out on a metabolism ward during control (4 to 5 weeks), immobilization (5 weeks), and recovery (5 to 6 weeks) periods. The dietary intake was constant. During the immobilization periods, the subjects were in bivalved plaster casts extending from umbilicus to toes. One year previously the three subjects studied had participated in an experiment identical with the present study except that they had been immobilized in standard (fixed) hospital beds. During immobilization in the oscillating bed:

(1) Nitrogen excretion increased in the same general pattern as in the fixed bed experiment; but in two of the subjects nitrogen loss was approximately half as great as during an equal period of immobilization in the fixed bed.

(2) The loss of calcium, chiefly in the urine, was, on the average, half as great as during the same period in the fixed bed.

(3) the loss of phosphorus was significantly less in two of the subjects than during the same period in the fixed bed.

(4) Although urinary citric acid, pH, and urine volume did not appreciably change, the significant reduction in urinary calcium and phosphorus losses would render the precipitation of calcium phosphate in the urinary tract less likely than during immobilization in a fixed bed.

(5) There was good correlation between the excretion of urinary total sulfur and nitrogen on the basis of the ratio in which they exist in muscle. The correlation between nitrogen and phosphorus on the same basis was less good, between nitrogen and potassium, poor.

(6) Creatine tolerance tests indicated that creatine metabolism was significantly less impaired than during immobilization in the fixed bed. The decrease in muscle mass and strength of the immobilized limbs was also less than during an equal period in the fixed bed.

(7) Changes in basal oxygen consumption were not significant.

(8) The deterioration produced by fixed-bed immobilization in the mechanisms essential for adequate circulation in the erect position (as measured by tilt-table tests) was largely prevented.

(9) Measurements of venous pressure in the foot veins during oscillation revealed an average change in pressure of 140 mm of water with each change in position of the bed. A rhythmical shift was observed in the average level of the diaphragm with each change in position of the bed, without significant alteration in the pulmonary minute ventilation.

(10) Changes in urinary 17-ketosteroid secretion and in serum calcium levels were not significant.

(11) As in the fixed-bed experiment, there were no significant alterations in blood coagulation studies, circulation time, heart size, or electrocardiograms.

During the recovery phase most metabolic and physiologic functions returned to control levels or became restabilized more rapidly than following immobilization in the fixed bed. Following recovery from the oscillating bed experiment, one subject was re-immobilized in a fixed bed for 2 weeks. The results duplicated closely the changes observed during the first 2 weeks of his first immobilization in a fixed bed a year previously.

262. White, P. D., J. W. Nyberg, L. M. Finney, and W. J. White. A comparative study of the physiological effects of immersion and bedrest. Rept. DAC-59226, Douglas Aircraft Co., Inc., Santa Monica, Calif., June 1966.

Purpose: To compare the physiological responses of 10 subjects, each serving as his own control, during alternate 10-day periods of immersion and bedrest. Fluid silicone was used as the immersion medium.

Authors' summary: Neither immersion nor bedrest produced appreciable changes in Master's two-step test of exercise tolerance, resting oxygen consumption, tolerance to acceleration in the $+G_z$ direction, visual and auditory acuity, or in ECG and heart sounds recorded during tilt-table testing. There were no significant changes in microscopic or qualitative analysis of the urine for sugar, acetone, or protein; resting blood pressure, temperature, heart, and respiration rate; blood and urine chemistries, or kidney and liver functions.

No serious complications were noted in any of the subjects during immersion or bedrest. Neither analog produced a free-water diuresis. The results of the study confirm the detrimental effects of prolonged immersion and bedrest on orthostatic tolerance and extracellular fluid volume. Both analogs brought about a deterioration in the mechanisms essential for adequate circulation in the erect position. This was shown by increased incidence of presyncopal reactions, by declines in pulse pressure, and by increased heart rate during tilt table testing. Experimental conditions produced reductions in plasma, blood, and extracellular fluid volumes; declines in maximum oxygen consumption; and some impairment of postural equilibrium. Losses in body weight were progressive, the average was approximately 2 percent of initial weight. A negative free-water clearance was obtained in all subjects during immersion and bedrest.

Differential effects of the two environments are seen in orthostatic tolerance, fluid compartments, and renal function. The incidence of presyncopal reactions was higher and occurred earlier during immersion than during bedrest. Heart rates were higher and pulse pressures were lower during immersion than during bedrest. After 5 days of immersion and bedrest, the extracellular fluid decreased by 3 and 2 percent, respectively. After 10 days, the net decrease in fluid was 5 percent during immersion and 7 percent during bedrest. The conditions of immersion produced a larger loss in plasma volume after 5 days than did bedrest, but the net loss after 10 days was approximately the same for both environments. Changes in blood volume were parallel to those of plasma volume. Immersion produced an elevated urine flow, as evidenced by a comparison of urine outputs in the two environments and by higher urine outputs than fluid intakes during immersion. During bedrest the subjects produced a more concentrated urine, both with respect to individual electrolytes and solute load. During immersion the daily solute load excreted by the kidney was higher, urine output was larger, and osmolar clearance was higher.

The silicone fluid, immersion tanks, filtration, and cooling equipment met the requirements of the experiment. Except for two subjects, skin problems that developed during immersion were trivial. An effort to relate the occurrence of skin problems to bacteria, water, and contamination of the silicone was inconclusive. During a 6-month period following the study, the subjects were free of abnormal physical signs, symptoms, and skin problems.

263. White, P. D., J. W. Nyberg, L. M. Finney, and W. J. White. Influence of periodic centrifugation on cardiovascular functions of man during bedrest. Rept. DAC-59286, Douglas Aircraft Co., Inc., Santa Monica, Calif., June 1966.

Purpose: To determine an optimal conditioning regimen of $+G_z$ acceleration to counteract the deconditioning of prolonged bedrest.

Authors' summary: A study was made of the influence of periodic centrifugation on the physiological disturbances associated with 10 days of bedrest. During bedrest the six subjects were scheduled to ride the centrifuge four times each day; the duration of each ride was 20 min; and the magnitude of acceleration was $+2.5\ G_z$ at heart level. Subjects exercised for a 14-day period before the study. The energy cost of this exercise was approximately 1000 kcal/day/man.

The prescribed regimen of $+2.5\ G_z$ for 20 min exceeded tolerance to positive acceleration. The modal conditioning regimen was $+1.75\ G_z$ for 20 min four times each day. When the magnitude of acceleration is referenced to foot level, the integrated G-time is 4.7 G- hr.

Expected deterioration produced by recumbency in the ability to tolerate 70° head-up tilt for 20 min was largely alleviated by periodic centrifugation, as judged by syncopal episodes and highest orthostatic heart rates.

The conditioning regimen did not appear so effective as shorter G-time integrals, as judged by highest orthostatic heart rates and plasma volumes.

Step-function acceleration tolerance and tolerance for sustained acceleration are more sensitive than the standard bioassay method for measuring cardiovascular changes at bedrest. Tolerance to positive acceleration declines during the first 12 hr of bedrest, remains relatively constant during bedrest, and improves during ambulation.

Losses in body weight were progressive and ranged from 0.98 to 2.35 kg. Average weight loss during the 10-day period was 2 percent. The condition of the experiment resulted in an average loss of 17 percent in total blood volume, 26 percent in plasma volume, and 2 percent in red blood cell volume. No significant changes were seen in serum electrolytes, bilirubin, glucose, or blood urea nitrogen; in red blood cell, white blood cell, or reticulocyte counts; in hemoglobin, hematocrit, or in mean corpuscular hemoglobin concentration; in hearing, or in the postural equilibrium; nor was there any change in exercise tolerance as measured by the Master's two-step test.

No cardiac irregularities or arrhythmias were encountered in the testing of eight subjects during a total of 135 hr of positive acceleration. Application of negative pressure to the lower half of the body produces cardiovascular changes similar to those seen in 70° head-up tilt. Application of a pressure differential of 70 mm Hg to subjects after 10 days of bedrest produced presyncopal symptoms in 2 to 4 min. During the prerecumbency period, these two subjects tolerated 20 min of negative pressure without symptoms.

264. Widdowson, E. M. and R. A. McCance. The effect of rest in bed on plasma volume: as indicated by haemoglobin and haematocrit levels. *Lancet* 1:539-540, 1950.

Purpose: To investigate the changes in serum proteins, hemoglobin, and hematocrit in patients changing from the vertical to the horizontal position.

Procedure and methods: Ten hospital patients (5 males, 5 females), whose complaints were not likely to have any effect on the volume or composition of their blood, were admitted to the hospital at noon and the first blood sample was drawn. Blood was collected subsequently at 2 hr and after 3 days, during which time the patients remained in the horizontal position. 1200 ml of water were given to 9 patients after 2 hr in bed and again after 3 days in bed.

Results:

	Hemoglobin (gm/100 ml)	Hematocrit (percent)	Serum proteins (gm/100 ml)
Control	14.1	44.7	7.58
After 2 hr	13.6	43.2	7.00
After 3 days	14.6	46.4	7.14

The net effect of 3-day recumbency was a rise in the hemoglobin and hematocrit levels above control values that very likely reflected a fall in plasma volume. The percentage changes in serum protein are about twice as great as those for hemoglobin and hematocrit. The changes in the serum protein followed the changes in hemoglobin and hematocrit much more closely over the shorter than over the longer periods of time. The average 5-hr urinary volume after the 2-hr water loading was 1268 and 1274 ml after the 3-day water loading. Though 3 days in bed reduced the plasma volume, it did not reduce the diuretic effect of water. After 2 hr in bed, there is an apparent rise in the plasma volume followed by a fall in plasma volume after 3 days.

Summary: When patients rested in bed for 2 hr their hemoglobin, hematocrit, and serum protein levels fell during the first 2 hr of recumbency, but if rest was continued for 3 days the levels rose again to their original height. It is suggested that this secondary rise in the concentration of the circulating elements may be the result of inactivity rather than recumbency. Even though 3 days in bed reduced the plasma volume, it did not reduce the diuretic effect of ingested water.

265. Williams, B. A. and R. D. Reese. Effect of bedrest on thermoregulation. Aerospace Medical Association Preprints 1972, pp. 140-141.

Purpose: To determine what changes occur in the thermoregulatory control system during the simulated weightlessness of prolonged bedrest, as determined by measurement of the sweating onset in response to an imposed heat load.

Procedure and methods: Eight male subjects were stabilized in a diet-controlled pre-bedrest period and then subjected to 14 days of complete bedrest followed by 14 days of recovery. This experimental profile was repeated twice.

Determination of the functioning of the thermoregulatory control system was made by imposing a heat load and measuring the latency and onset of the sweating response on the calf. The standardized heat load was imposed by placing the subjects, supine, into an environmental room and raising the air temperature to 41°C T_{DB}. Local sweating onset was measured on the calf. Dried air was passed through the capsule at a rate of 1500 cc/min and any increase in water content of the air was measured as an increase in the dew point which was continually recorded. The sweating onset was recorded as a sudden increase in water content of the airstream.

In addition to the sweating onset, 10 skin temperatures, rectal temperature, ear canal temperature, heart rate, and chamber thermal and humidity conditions were recorded continuously. Each subject was exposed to the heat load twice during each experiment segment. Subjects were tested in the supine position during all segments of the experiment.

Results: During the bedrested period, the onset of sweating occurred at a lower mean skin temperature (T_{MS}) than during the control and recovery periods. The means of the calculated T_{MS} at the onset of sweating became significantly ($p < 0.001$) different using analysis of variance techniques. Normalized T_{MS} determination show an even greater difference between the mean T_{MS} values. A decrease in rectal (core) temperature on exposure to the heat load was interpreted as an indication of the reflex movement of core blood to the peripheral tissues in order to enhance heat loss (vasodilitation). The drop in rectal temperature in response to the heat load was not as great during bedrest.

Conclusions: An effect of prolonged bedrest on the thermoregulatory system is evident during an imposed heat load. The threshold for sweating occurred at a lower mean skin temperature and the normal vasodilation response appears to be impaired slightly. It is possible that the result of bedrest is to decrease the circulatory capability of the body (autonomic dysfunction) and the effect on the thermoregulatory system therefore is to decrease vasomotor heat-loss capability.

266. Winget, C. M., J. Vernikos-Danellis, S. E. Cronin, C. S. Leach, P. C. Rambaut, and P. B. Mack. Circadian rhythm asychrony in man during hypokinesis. *Journal of Applied Physiology* 33:640-643, 1972.

Purpose: To evaluate the influence on healthy human subjects of the removal of endogenous synchronizers by 56 days of hypokinesis on circadian wave form in an environment with well-defined exogenous synchronizers.

Procedure and methods: Eight male subjects were subjected to a 6-day pre-bedrest control period, 56 days of bedrest and a 10-day ambulatory recovery period. During bedrest, four subjects exercised isokinetically (Exergenie) three times a day. Each exercise period consisted of 20 min of isotonic and 30 sec of isometric exercise with an estimated expenditure of about 800 kcal/day.

There were 14 hr of light and 10 hr of dark, and ambient temperature was $20° \pm 1°C$.

The subjects ate an Apollo diet regulated at approximately 2600 kcal/day. Body weight remained essentially constant throughout the study.

Measurements taken were heart rate, ear-canal temperature, plasma thyroid hormones (T_3, T_4), and plasma corticosteroid concentration.

Results: With mean data from all eight subjects, bedrest did not affect the ear-canal temperature wave form but it produced a depression of mean body temperature that did not return to pre-bedrest levels. Bedrest had no effect on the heart-rate wave form. The daily range of body temperature was about 1°C and heart rate about 15 beats/min.

All subjects had well-defined heart-rate circadian rhythms. During bedrest, the nonexercise group had a less stable circadian oscillation than the exercise group. The phase of the heart-rate rhythm of the two groups did not change appreciably throughout the study.

During the control period all subjects exhibited a stable phase and amplitude of their body temperature rhythms. During bedrest there was a tendency for the temperature rhythms to become desynchronized with the environment although this rhythm remained circadian.

There was a stable phase relationship between body temperature and corticosteroids, between heart rate and corticosteroids, and between body temperature and heart rate. On the other hand there were changes in the phase relationships between T3, T4, and the other circadian parameters. Exercise did not affect the nature of these relationships. The circadian fluctuations in heart rate have less day-to-day variation than the body temperature.

Conclusions: Some factor or group of factors present during bedrest, with its influence persisting for at least 10 days after bedrest, affected both ear-canal temperature and heart-rate periodicity by reducing the amplitude and changing the phase-angle relationships; in effect, bedrest induced a low-grade hypothermia and a minor tachycardia.

The exercise schedule had little influence on the physiological parameters measured in this study.

The mechanism regulating the circadian rhythmicity of the cardiovascular system is rigorously controlled and independent of a portion of the endocrine system, while the ear-canal temperature rhythm is more closely aligned with the endocrine system.

267. Yakoleva, I. Ya., V. P. Baranova, L. N. Kornilova, M. V. Nefedova, E. V. Lapayev, and S. R. Raskatova. Study of reactions of human otorhinolaryngological organs during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 6:49-54, 1972.

Authors' abstract: The results of a study of the functional state of otorhinolaryngological organs during a 30-day antiorthostatic bedrest experiment are presented. The test subjects included three groups of three men each. The subjects in the first group performed physical exercises while remaining in bed, those in the second group were used as controls, and the subjects in the third group were subjected to electric muscle stimulation. The test subjects underwent special examinations which included audiometric, ototopical, rhinopneumometric, and otolithometric studies and spatial perception measurements. Dynamic rhinopneumometry revealed increased blood filling of the vessels in the nasal mucosa and lability of their tone in the test subjects of all three groups, the highest level being noted in the controls. Audiometric examinations revealed similar changes in the functions of loudness and ototopics in all test subjects. Investigations of hearing thresholds demonstrated appreciable changes in subjects suffering from early cochlear neuritis. The test subjects exhibited the greatest errors in spatial perception during the first hours of hypokinesia and during the first days after the experiment. During the course of the experiment the subjects in the second and third groups exhibited only a tendency to an increase in errors in spatial perception. Otolithometric investigations also revealed certain differences varying from group to group. The controls exhibited the greatest changes in the degree of the otolithic reflex.

268. Yakovleva, I. Ya., V. P. Baranov, and E. I. Matsnev. Effect of prolonged hypokinesia on certain functions of the otorhinolaryngological organs. *Vestnik Otorinolaringologii* 6:45-51, 1967.

Purpose: To investigate the functional state of the ear, nose, and throat organs during prolonged bedrest.

Procedure and methods: Six healthy men (22 to 36 yr) were used as subjects and most had engaged in sports. They remained in bed for 62 days and three men were non-exercise controls. Ambient humidity was 40 to 60 percent.

The exercise group performed 15-30 min of work in the morning and 1 to 2 hr of work in the afternoon at an intensity of 600-1200 kg-m/min. The work duration was gradually increased during the first 30 days and during the last 32 days the intensity was increased.

The training was performed utilizing springs and large rubber bands. Bands with resistances of 7.5 to 15 kg were used to exercise the shoulder muscles and bands between 15 and 50 kg were used for the lower extremities. The bands were used for isotonic and isometric (static) exercise. The average energy cost of the exercises was about 7.3 kcal/min (500 to 1000 kcal/day) with a total working time of 75 to 150 min/day.

The calorie intake was 3000 to 3500 kcal/day.

Audiometry and rhinopneumometry were performed at 4- to 6-day intervals during bedrest. Vestibulometry was measured before and after bedrest to test for tolerance to Coriolis accelerations.

Results: There was an increase in the dystrophy of the mucosa of the upper nasal passages. Nasal hemorrhages occurred in four subjects during bedrest. There was swelling of the lower nasal sinuses and the mucosa showed a moderately pronounced bluish coloring.

There was an increase in intranasal drag suggesting an increase in blood flow in the nasal mucosa (on the 5th, 8th, and 10th day of bedrest). Nasal function was better in those subjects performing physical exercise. The reaction of the nasal vascular system to change in body position after bedrest was more strongly pronounced, especially in the non-exercising subjects. The recovery period for the non-exercising subjects was about 13 days but only 1 to 2 days for the exercise group.

The threshold sensitivity for auditory acuity was raised from 15 to 34 db in all subjects; the audibility thresholds increase mainly for high frequencies (2000 to 8000 Hz). Audibility thresholds returned to normal immediately in four subjects, but after 2 weeks in two subjects. Exercise had no effect on auditory sensitivity.

All subjects showed deterioration in tolerance to the vestibular tests. Exercise had no obvious effect on vestibular sensitivity. Autonomic reactions to the Coriolis acceleration tests were much more pronounced after bedrest. Recovery of initial responses to the Coriolis test took 14 days in two subjects, 55 days in one subject, and had not returned to normal after 75 days of recovery in two subjects.

Conclusions: Restriction of mobility and relative isolation for 2 months in generally healthy persons causes a number of functional disturbances.

Changes in lower organs are characterized by disturbance of blood circulation in the nasal mucosa, reduction in auditory sensitivity, and reduction vestibulo-autonomic resistance exhibited undulant dynamics and a period of sequelae. The factor of asthenia is significant for these changes, to some extent caused by general hemodynamic shifts.

Disturbances in intranasal blood circulation were in the form of congestive symptoms in the inferior nasal sinuses and lability of their vascular tonus; greater intensity of these disturbances was noted in the group without physical exercises.

Fluctuations in the auditory thresholds during the hypokinesia period amounted to 15-34 db, mainly at high frequencies, and were the same in both groups. When cochlear neuritis was present, hearing was found to be less resistant to hypokinesic factors.

The decrease in vestibulo-autonomic resistance after hypokinesia was differentiated in character, and the tolerance to cumulation of Coriolis accelerations was disturbed for a longer time compared with tolerance to the cumulation of linear accelerations. Vestibular disturbances were more well defined in the group of subjects not performing physical exercises.

Hypokinesia promoted an increase in the dystrophy of the mucosa of the upper respiratory passages and reduced resistance of the organism, which possibly also was responsible for the development and aggravation of pathological processes in the ORL organs.

269. Yakovleva, I. Ya. and E. I. Matsnev. Functional state of the human auditory analyzer in an experiment with two-month hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 1:66-70, 1967.

Authors' abstract: A study of the functional state of the human acoustic analyzer was carried out during a 2-month exposure of test subjects to hypokinesia. The test subjects were six healthy men aged 22-36 yr. The effect of hypokinesia was brought about by strict bedrest. The experiments revealed transient functional impairments of hearing which resulted in an increase of the thresholds from 15 to 34 db. The changes may be attributed to disturbances of the central nervous system and circulation causing hemostasis in the inner ear.

270. Yarullin, Kh. Kh., T. N. Krupina, T. T. Vasil'yeva and N-N. Buyvolova. Changes in cerebral pulmonary and peripheral blood circulation. *Kosmicheskaya Biologiya i Meditsina* 6:33-39, 1972 (see paper by Voskresenskiy *et al.,* 1972).

Purpose: To investigate the circulation in man during 30 days bedrest with the head of the bed angled downward 4°.

Procedure and methods: Nine men (10 to 33 yr), the series B subjects, were bedrested for 30 days with the head of the bed angled 4° downward. Three subjects performed isotonic exercise on a vertical treadmill, three subjects were the no-exercise control group, and three subjects were given electric stimulation of their trunk muscles (isometric exercise).

Blood flow was measured with two transistorized, four-channel rheographs, utilizing an a-c demodulating bridge at a working frequency of 120 kHz, current strength of 2.5 mA and 3 V. The condition of blood filling, elasticity and tone of the cerebral pulmonary and peripheral vessels was determined from data from both a physical evaluation and a quantitative analysis of the rheograms.

Results: Six hours after bedrest began, in all nine subjects there was increased blood flow to the brain and lungs. There was considerable decrease in tone of the small and intermediate caliber cerebral veins and an increased tone of the pulmonary vessels. These symptoms of vasodilatation, arterial and venous hypotonia, accompanied by a considerable increase in cerebral blood filling, became more intensified on the second and third days of bedrest. Blood filling of the vessels of the hand and skin increased gradually from the first day and by the third day had increased 50 to 70 percent compared with control values. These hemodynamic shifts were caused by a decrease in vascular tone.

By the end of the first week the subjective and objective symptoms of arterial and venous plethora in the head and brain had decreased and was essentially normal by the 10th day in the isotonic exercise group but reappeared in the no-exercise control group. It took nearly 30 days for the cerebral circulation to return to pre-bedrest levels. At 30 days the peripheral circulation showed a marked decrease in tone and was still unstable.

Conclusions: During 30 days of bedrest with downward tilting of the head, it was the functional state of the arterioles and veins that was most impaired. The greatest impairment of the circulation was observed in the no-exercise group, moderate impairment in the isometric group, and least impairment in the isotonic exercise group.

The difference in hemodynamic shifts, including cerebral, between the subjects in the isotonic exercise group and the no-exercise group can be attributed to the greater cardiac stroke volume with exercise.

The changes in hemodynamics observed during the first week of bedrest, particularly the overfilling of the lungs and brain, were caused by overloading of the lesser circulatory system as a result of an increase of incoming blood and difficulties with blood outflow from the head and lungs, together with venous stagnation in the brain. Adaptation of the circulation under these circumstances takes about 30 days.

271. Yefimenko, G. D. Functional state of the central nervous system during prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:123-132, 1969.

Author's abstract: Rheoencephalography brought out consistently directed shifts in the hemodynamics of the brain in all subjects: a decrease in the blood-filling index and vascular tone index, shorter propagation times of the rheographic wave, and increased lability of the hemoregulatory nerve centers. Signs of the functional disturbances to the central nervous system that are characteristic of neurotic states were observed on the survey electroencephalograms of all subjects. There was apparently no decrease in the short-term fitness of the subjects for light mechanized labor during the 75 days of hypodynamia. Analysis of the indicators for each individual subject indicates phasing of the changes during the prolonged hypodynamia.

272. Yegorov, P. I., K. V. Smirnov, M. M. Korotayev and M. V. Lukasheva. Effect of acceleration and hypokinesia on the functional state of the stomach. *Kosmicheskaya Biologiya i Meditsina* 1:71-74 1967.

Purpose: To study the effect of acceleration and hypokinesia on the secretions of human gastric glands.

Procedure and methods: Five healthy male subjects 23-36 yr were exposed twice to chest-to-back accelerations of 11.9 – 14.5 G with an interval of 4-6 days. The subjects were then kept in bed for 62 days; during this time two subjects performed allotted physical exercises without leaving the horizontal position. The other three subjects had no physical load. Immediately after the period of hypokinesia, there were two tests on the centrifuge with 2 weeks intervening at a maximum transverse overload of 11 to 16 G. During the whole experiment the subjects were fed four times a day (3500-4000 cal) – proteins, 120 gm; fats, 100 gm; and carbohydrate, 450 gm. Gastric secretion was studied by fractional testing with a fine probe on an empty stomach in the morning. Gastric juice was analyzed for total and free acidity and pepsin. Gastric juice was taken before the experiment started, 20 hr after the first centrifuge test, the 3rd day after the second centrifuge test, on the 10th, 30th and 55th days of bedrest, and on the 3rd, 13th day, and 1 month after bedrest.

Results: During the whole experiment, which totaled 4 months, a significant depression of the juice-secreting function of the stomach was observed: 30 percent reduction 20 days after the centrifuge test, 35 percent on the 3rd day after repeated centrifuge test, 45 percent on the 30th day of bedrest, and 40 percent after bedrest. Total and free acidity was elevated 20 hr after the acceleration and remained high on the 3rd day after the repeated acceleration and on the 30th day after the experiment it had not returned to its original values. The subjects who had no physical load had an even greater rise in total and free acidity. The pepsin level fell 70 percent 20 hr after centrifugation and remained depressed until the 10th day of bedrest when it drastically increased. In the following days of the experiment the pepsin reduced about 60 percent and remained low throughout the observed time.

Conclusions: The exposure to accelerations inhibited the secretory and exzyme-forming gastric functions. The acidity of the intestinal juice showed a tendency to increase. Hypokinesia conditions produce further inhibition of the glandular apparatus of the stomach.

273. Yeremin, A. V., V. V. Bazhanov, V. L. Marishchuk, V. I. Stepantsov, and T. T. Dzhamgarov. Physical conditioning for man under conditions of prolonged hypodynamia. *Problemy Kosmicheskoy Biologii* 13:192-199, 1969.

Purpose: To investigate the effect of various physical exercise regimes on bedrest deconditioning.

Procedure and methods: Sixteen healthy male (21 to 23 yr) volunteers were divided into five groups and underwent 70 days of bedrest. The subjects were tested before, during (70 days), and after (21 days) bedrest. Group I (subjects K-s, K-n, M-s, Ch-y) was the control and was given no remedial procedure. They were forbidden to turn over on their stomachs or raise their heads from the pillow. Group II (subjects B-k, B-y, G-y) received cardiovascular and nervous system stimulants (amphetamine, securinine, caffeine) on a 4-day cycle with 9 to 16 days between cycles. Group III (subjects K-v, M. M-k, V. M-k) were give treadmill exercises with addition of autogenous conditioning elements. Group IV (subjects B-v, A-v, K-ya) exercised on a bicycle ergometer while remaining in the horizontal position. Group V (subjects A-n, L-i, F-v) exercised on a treadmill. Groups IV and V were given identical occlusion conditioning on a cyclic basis during weeks 4-5, 7-8, and 9-10. This conditioning consisted of application of aircuffs to the upper third of the thighs with pressure of 75 to 80 mm Hg at 1-min inflation and 1-min rest intervals for an unspecified period each day. These two groups were also given orthostatic tolerance tests on a tilt-table during weeks 3-4 and 7-8. Before centrifugation these subjects were given drugs.

Results: Physical conditioning solved the following problems: (a) it preserved orthostatic stability and responses to centrifugation after bedrest; (b) prevention of abnormalities in body composition and bone structure; (c) maintenance of muscular strength and endurance under dynamic and static physical loads; preservation of movement coordination (especially in walking and running), quickness of actions and attention; and (d) securing a general tonic effect on the nervous, cardiovascular, digestive, and other systems of the organism.

Authors' conclusions: It was found as a result of the studies that definite changes took place in the physical condition of the subjects under the conditions of artificial restriction of motor activity and prolonged confinement to the supine position, taking the form of deteriorated functional condition of the organism as a whole and, in particular, of the cardiovascular system and supporting-motor apparatus.

After 70 days of the hypodynamic regimen, the subjects who did not engage in physical exercises were unable to move about by themselves. Where physical exercises were performed, all of these changes, and primarily that in the physical state of the subjects, were much less pronounced especially as regards retention of the strength of various muscle groups, static endurance, preservation of locomotor coordination habits, and various psychomotor functions.

The cardiovascular systems of the subjects remained more efficient, and the effects of vascular insufficiency were less pronounced on transition from the horizontal to the vertical position and on transition from exertion to rest and rest to exertion.

Emotional stability also fared better, as did efficiency under emotional stress and the sthenic emotional state.

No marked differences in either the psychomotor functions or the stability of the psychic functions were observed between the groups of subjects who exercised on the treadmill and on the bicycle ergometer, although group 1 had certain advantages as regards physical condition and preservation of walking coordination habits.

In addition, the "treadmill" appliance scores better than the bicycle ergometer both methodologically and in the sense of emotional attractiveness of the exercises.

274. Zager, P. G., G. A. Melada, R. H. Goldman, C. M. Gonzales, and J. A. Luetscher. Increased plasma renin activity (PRA) in prolonged bedrest. *Journal of Clinical Endocrinology* 53:87a, 1974.

Authors' abstract: The circadian rhythm of PRA in normals rises episodically during early morning, falling during the afternoon and evening in recumbent normals. Standing evokes a rise in PRA, which falls with recumbency. We studied the diurnal variation of PRA in five normals on constant diet (NA 130, K 90 meq/day) during normal daily activity and after 3-12 days of continuous bedrest. Unexpectedly, bedrest was followed by a marked rise in PRA during the morning. The lowest PRA was found at 8 a.m. and 11 p.m. during the ambulatory period, and the maximum occurred at noon. After 3-12 days of continuous bedrest, PRA at 8 a.m. was three times the control and remained as high at noon as after a morning of standing. Neither 5 p.m. nor 11 p.m. PRA values during bedrest differed from the ambulatory controls. Renal blood flow (PAH) and glomerular filtration rate (inulin) were unaffected by bedrest. Plasma angiotensinogen levels were also unchanged. Although plasma volume may fall during bedrest, extracellular fluid volume was increased by an average of 2 liters. Cardiac output and blood pressure were not altered. With resumption of normal activity, standing evoked exaggerated rise in PRA. Marked increases in PRA were observed in hypertensive patients after 32 hr of bedrest. We conclude that prolonged bedrest enhances the circadian peak of renin during the early morning hours and increases the rise of PRA when upright posture is resumed. This effect must be considered in evaluating PRA in normal men and in hospitalized hypertensive patients.

275. Zav'yalov, Ye. S. and S. G. Mel'nik. The scanning activity of a man operator exposed to space flight factors. *Kosmicheskaya Biologiya i Meditsina* 1:57-62, 1967.

Authors' abstract: A 10-day period of hypokinesia of a man operator resulted in a deterioration of his compensatory scanning. His control habits were restored by daily training by the third day after exposure to hypokinesia. The relationship between the control habits and the level of hypoxia and hypercapnia was determined. Scanning habits were significantly impaired when the man operator was exposed to atmosphere containing 8.2 percent O_2. Breathing air with a CO_2 content of 7.2-8.6 percent resulted in a transient deterioration of his scanning activity. At a CO_2 concentration of 9-9.2 percent the activity remained impaired throughout the hypercapnia effect.

276. Zav'yalov, Ye. S., S. G. Mel'nik, G. Ya. Chugunov, and A. A. Vorona. Performance of operators during prolonged bed confinement. *Kosmicheskaya Biologiya i Meditisina*. 4:61-65, 1970.

Purpose: To study the effect of isometric and isotonic exercise during 100 days bedrest on flight-control skills.

Procedure and methods: Six trained control system operators were divided into two groups of three subjects each. One group performed a groups of isometric and isotonic exercises involving the principal muscle groups of the body every fourth day during bedrest. Two additional trained operators served as ambulatory controls. Two control tasks were used. The first task simulated the dynamics of manual control of flight-vehicle angular accelerations. The task was programmed by a computer and the full cycle took less than 40 sec. The second task reproduced some control elements performed by a flyer while flying a course at a particular attitude.

Results: On the first task the efficiency of the control operators not exposed to bedrest was 1.2, for the exercise group 2.6, and 5.4 for the non-exercising subjects, indicating substantial decrements in performance. On the second task the subjects not performing the exercises had lower efficiency than the exercising subjects.

Conclusions: Operator control skills of the scanning type requiring finely coordinated and precise oculomotor movements deteriorate considerably during 100 days of bedrest. Loss in control efficiency is associated primarily with lack of physical exercise. Physical exercises during bedrest favor the retention of skills which require fine oculomotor coordination.

277. Zhdanova, A. G. Macrometric changes in the makeup of the human body in hypodynamia. *Arkhiv Anatomii, Gistologii i Embriologii* 49:29-34, 1965.

Purpose: To investigate the effect of hypodynamia on changes in body composition as measured by its specific gravity.

Procedure and methods: Eighteen men (20 to 25 yr) underwent bedrest or water immersion. Ten men were subjected to bedrest for 2 days (1 man), 5 days (2 men), 7 days (3 men), and 10 days (2 men). Eight men were subjected to water immersion for 2 days (4 men), 5 days (3 men), 7 days (1 man), and 10 days (2 men). Body specific gravity was determined by hydrostatic weighing.

Results: There was a general increase in the body fat content after 2 days bedrest or water immersion–average of 250 gm, and 1030 gm after 7 days, and 1440 gm after 10 days; and a decrease in the nonfat (lean body mass) component.

278. Zhidkov, V. V., V. V. Borschenko, G. N. Komzalova, and G. A. Vavilkina. Peculiarities of human skin reactions to lotions of different composition during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 7:83-86, 1972.

Authors' abstract: The irritating effect of different lotions and distilled water on the human skin was demonstrated in a 30-day bedrest experiment, the irritation increasing with the length of exposure to hypokinesia. The L-211 lotion was better tolerated than the other lotions tested. When recommending the use of various means of personal hygiene for manned space flights, it is necessary to take into account the hypokinetic effect, which may increase skin hyperergic reactions.

279. Zubek, J. P. Counteracting effects of physical exercices performed during prolonged perceptual deprivation. *Science* 142:504-506, 1963.

Author's abstract: Subjects who were required to perform physical exercises during a week's exposure to unpatterned light and white noise showed fewer impairments on 15 behavioral measures than did subjects who were not required to exercise during the same period in an isolation chamber. Furthermore, fewer hallucinatory phenomena and fewer disturbances of the electroencephalogram were observed.

280. Zubek, J. P. Urinary excretion of adrenaline and nor-adrenaline during prolonged immobilization. *Journal of Abnormal Psychology* 73:223-225, 1968.

Purpose: To determine the effect of partial immobilization and confinement in the horizontal position for 7 days on urinary excretion of catecholamines.

Procedure and methods: Twenty-six male university students were immobilized in a coffin-like box, under normal conditions of visual and auditory stimulation for 1 week. A second group of 16 recumbent control men were placed in a twin immobilization box for 1 week, but they were not placed in the coffin-like box.

Urine samples were taken at 24-hr intervals for 3 days prior to the experiment, at daily intervals during bedrest, and for 2 days after. Another 24-hr urine sample was taken 2 months after the completion of the study.

Adrenaline and noradrenaline were expressed as total excretion per 24 hr. An appraisal was made of the subjects' affective state by having them take the Subjective Stress Scale of M. M. Berkin et al. and the Myers Mood Scale by T. I. Myers et al.

Results: Those subjects who completed the period of immobilization and the recumbent controls showed a significant decrease in urinary adrenaline and noradrenaline excretion during the bedrest period. Those subjects who withdrew early from the immobilization showed an increase in noradrenaline and particularly in adrenaline excretion after the second day of bedrest. Another characteristic of the quitters was the presence of a lower control level of both catecholamines and also after 2 months of recovery. The results of the two written tests showed no difference between those who successfully completed the bedrest and the recumbent control subjects. However, the quitters showed a significant increase in the stress score and a more negative mood.

281. Zubek, J. P., M. Aftanas, K. Kovach, L. Wilgosh, and G. Winocur. Effect of severe immobilization of the body on intellectual and perceptual processes. *Canadian Journal of Psychology* 17:118-133, 1963.

Authors' summary: The purpose of the experiment was to determine whether severe restriction of kinesthetic stimulation alone will produce any of the typical sensory and perceptual deprivation phenomena. A group of 40 subjects were strapped into a specially constructed box which prevented movements of the limbs, trunk, and head for a period up to 24 hr. No restrictions were placed on visual and auditory stimulation. A battery of seven intellectual tests and eight perceptual-motor tests was administered before and immediately after the immobilization period. A questionnaire was also given. A group of 40 recumbent and 40 ambulatory control subjects were also given the same tests at the same time intervals.

An analysis of the questionnaire data revealed that the immobilized subjects reported a significantly greater incidence of intellectual inefficiency, bizarre thoughts, exaggerated emotional reactions, time distortions, changes in body image, unusual bodily sensations, and various physical discomforts than did the recumbent control subjects. Hallucinatory phenomena, although present, were rare. On the perceptual-motor tests, there was a significant impairment of dexterity, kinesthetic acuity, colour discrimination, and reversible figures. Perception of simple patterns was also affected to some degree. Pain sensitivity, tactual acuity, and a test of cancellation of figures were not affected. None of the tests of the intellectual battery were impaired.

It is concluded that reduction of kinesthetic stimulation alone can produce behavioral changes similar in many respects to those occurring under reduced visual and auditory stimulation. There are, however, a number of differences.

282. Zubek, J. P., L. Bayer, S. Milstein, and J. M. Shephard. Behavioral and physiological changes during prolonged immobilization plus perceptual deprivation. *Journal of Abnormal Psychology* 74:230-236, 1969.

Authors' abstract: The subjects who successfully completed 1 week of immobilization plus perceptual deprivation (IPD group) showed a greater slowing of occipital EEG activity and a poorer performance on a battery of intellectual and perceptual-motor tests than did subjects exposed to a similar duration of either immobilization (I group) or a recumbent control condition (RC group). During the 1-week period the IPD group also showed a significant increase in urinary excretion of noradrenaline, but not of adrenaline, relative to the I and RC groups. No significant differences were observed on behavioral measures of subjective stress and mood.

283. Zubek, J. P. and M. MacNeill. Effects of immobilization: behavioural and EEG changes. *Canadian Journal of Psychology* 20:316-336, 1966.

Purpose: To separate the psychological effects of immobilization from those resulting from the horizontal body position.

Authors' abstract: Two experiments were conducted to determine the effect of restricted motor activity, of a week's duration, on the electrical activity of the brain and on various measures of intellectural and perceptual-motor processes. The results of the first experiment showed a post-immobilization slowing of occipital EEG activity, an effect which was significantly different from that of both ambulatory and recumbent control subjects. In addition to this physiological change, a variety of behavioral deficits were found to occur (verbal fluency, recall, space relations, cancellation, reversible figures, and color discrimination). Some of these were associated with immobilization alone, while others appeared to be related to the combined effects of restricted motor activity and the recumbent position. In the second experiment, measures were taken of some of the more complex intellectual and perceptual-motor processes, namely, creative and critical thinking, and visual and auditory vigilance. None of the intellectual measures was affected. The results on the two vigilance tasks were unexpected. Performance on visual vigilance was significantly better after the week of immobilization. On the other hand, auditory vigilance was significantly worse in the recumbent subjects relative to the immobilized and ambulatory control subjects. A wide range of unusual subjective phenomena were experienced by the immobilized subjects. Almost all of these, however, could be atrributed to the recumbent position. Only the increased incidence of body-image disturbances and of boredom was associated with immobilization alone. These findings indicate that a reduction in the level of kinesthetic and proprioceptive stimulation via immobilization of the body can produce behavioral and physiological changes similar in many respects to those occurring after prolonged sensory and perceptual deprivation. The differences which occur lie largely in the magnitude of the effects.

284. Zubek, J. P. and L. Wilgosh. Prolonged immobilization of the body: changes in performance and in the electroencephalogram. *Science* 140:306-308, 1963.

Purpose: To determine the effect of reduction of only tactile and kinesthetic stimulation on the electroencephalogram and various performance tests.

Procedure and methods: Twenty-two male university students were placed for 7 days in a coffin-like box lined with foam rubber cut in the shape of a human figure. The legs and trunk were immobilized with belts. The subjects were unstrapped for 15 min at mealtimes, for 1 hr in the afternoon, and for 9 hr during the night, but during the latter they were not allowed to sit or stand up.

The subjects were given two batteries of tests: intellectual and perceptual. The intellectual tests measured 12 different abilities and consisted of simple arithmetic, mathematical reasoning (solving numerical sequences), abstract reasoning (solving sequences of patterns), verbal fluency (writing words beginning with a certain letter), verbal reasoning, space visualization, digit span, rote learning of a list of nine 3-letter words, word recall, word recognition, cancellation test, and manual dexterity. The battery of fine perceptual-motor tests was given only before and after immobilization and consisted of depth perception (Howard-Doklinan apparatus), size constancy, reversible figures, color discrimination (Farnesworth-Muncell test), and pain sensitivity (Hardy, Wolff, Goodell dolorimeter). Electroencephalograms were measured before and after immobilization. The preimmobilization results of the 22 immobilized subjects were matched with the initial scores of 22 out of 40 control subjects.

Results: All 22 subjects successfully completed the week of immobilization. The mean performance of the test subjects during immobilization was worse than that of the controls on all 12 intellectual tests. Of these tests, cancellation, recall, and verbal fluency were significantly impaired; space visualization and numerical reasoning bordered on statistical significance while the decreased scores for verbal and abstract reasoning, digit span, arithmetic problems, rote learning, and recognition were not significantly different.

Of the five perceptual-motor tests, color discrimination and reversible figures were significantly impaired; while depth perception, pain sensitivity and size constancy were not affected.

After immobilization there was a mean decrease in occipital lobe frequencies of 0.56 cycles/sec while the control subjects showed a mean difference of only +0.01 cycles/sec. Hallucinatory-like phenomena were quite rare.

Conclusions: The reduction of tactile-kinesthetic stimulation plus a reduction in circulatory hydrostatic pressure and energy output via immobilization produces disturbances of both performance and the electrical activity of the brain that are not caused by visual or auditory restrictions. Restriction of movement, particularly in infancy, may produce some degree of intellectual retardation.

285. Zvonarev, G. P. Dynamics of minute blood volume during prolonged hypokinesia as estimated by the acetylene method. *Kosmicheskaya Biologiya i Meditsina* 5:50-53, 1971.

Author's abstract: The minute blood volume of six healthy male test subjects was studied by the Grohlmann acetylene method. By the end of the bedrest experiment the minute volume had declined significantly for all the test subjects. In comparison with the test subjects who performed physical exercises during the experiment, the test subjects exposed to complete hypokinesia exhibited a greater (threefold) decrease in minute and stroke volume. The mechanism underlying the decrease in stroke volume is unrelated to pulse-rate variations. It appears to be related to changes in the cardiac contraction phases, blood flow velocity, and circulating blood volume. The minute volume decrease came about with a decrease in oxygen consumption in the subjects exposed to maximum hypokinesia and an increase in the arteriovenous difference in the test subjects who were allowed physical exercises.

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INDEX OF TERMS

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